Supporting Information

Asymmetric Total Synthesis of (+)-Fusarisetin A via the Intramolecular Pauson-Khand Reaction

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General Information

All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF and dioxane were distilled from sodium-benzophenone, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically, unless otherwise stated.

Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Tsingdao silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. Tsingdao silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography.

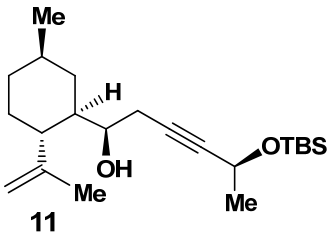
Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded on either a Brüker Advance 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), Brüker Advance 500 (^{1}H: 500 MHz, ^{13}C 125 MHz) and Brüker Advance 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz). Mass spectrometric data were obtained using Bruker Apex IV RTMS. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad.

Synthesis of Epoxides 12 and 12a:[1]

To a solution of aldehyde **16**[1] (1.65g, 9.93 mmol, 1 equiv) and chloroiodomethane (0.8 mL, 10.9 mmol, 1.1 equiv) in THF (26 mL) at -78 °C was added dropwise *n*-BuLi (1.45 M in hexanes, 0.72 mL, 10.4 mmol, 1.05 quiv). The resulting slightly yellow mixture was sealed under nitrogen and stirred for 24 h while allowing the bath temperature to rise to room temperature. The reaction was then quenched by addition of saturated aqueous NH_4Cl solution and the product was extracted with ether. The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated to an oil. Silica gel chromatography eluting with 1:1 benzene-hexanes afforded the pure diastereomer **15** (1.02 g) in 70% yield.

Reference:
1: E. J. Corey, D. D. Staas, *J. Am. Chem. Soc.* **1998,** *120,* 3526-3527.

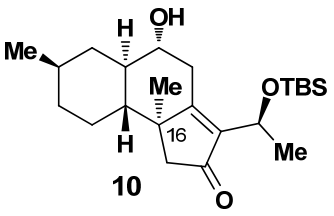
Synthesis of Compound 11:



11

To a solution of alkyne **14** (226.0 mg, 1.22 mmol) in freshly distilled THF (5 mL) was added *n*-butyllithium (0.16 mL of a 2.5 M solution in hexanes, 1.22 mmol) at -78 °C in a dropwise manner, and the mixture was stirred at the same temperature for 45 min. the mixture was then warmed up to -10 °C for 30 min, and then cooled back to -78 °C. To a solution of epoxide **12** (200mg, 1.11 mmol) in THF (5 mL) was added the solution prepared above via a cannular at -78 °C, followed by addition of $BF_3{\cdot}OEt_2$ (0.16 mL, 1.11 mmol) within 20 min. The resultant mixture was then stirred at -78 °C for 2 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (10 mL), and the mixture was extracted with ether (3 x 10 mL). The combined organic layers were washed with brine (5 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel. (hexane:ethyl acetate = 50:1) to give alcohol **11** (242.2 mg) as colorless oil in 60% yield; $R_f = 0.71$ (silica gel, EtOAc/hexanes = 1/6); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.77 (d, *J* = 9.8, 2H), 4.50 (d, *J* = 6.2, 1H), 3.79 (s, 1H), 2.46 – 2.40 (m, 1H), 2.32 – 2.26 (m, 1H), 2.12 – 2.06 (m, 1H), 1.69 (d, *J* = 9.4, 2H), 1.66 (s, 3H), 1.62 (d, *J* = 12.3, 3H), 1.56 (d, *J* = 11.9, 1H), 1.45 – 1.39 (m, 2H), 1.37 (s, 3H), 0.92 (d, *J* = 6.7, 3H), 0.89 (s, 9H), 0.10 (d, *J* = 5.3, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 148.82, 111.76, 84.88, 80.60, 70.11, 59.31, 48.16, 42.37, 34.93, 32.57, 32.42, 32.08, 25.98, 25.85, 24.98, 23.00, 18.42, -4.48, -4.74; HRMS (ESI) m/e 387.2683 [M+Na^+] calcd for $C_{22}H_{40}NaO_2Si^+$: 387.2690.

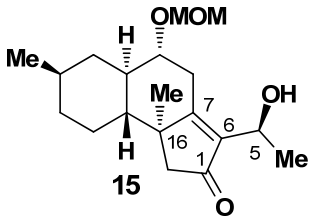
Synthesis of Compound 10:



10

To a solution of $Co_2(CO)_8$ (286.0 mg, 0.839 mmol) in dry PhMe (10 mL) was added a solution of compound **11** (278.0 mg, 0.762 mmol) in PhMe (10 mL) in a dropwise manner, and the resultant mixture was stirred at 120 ^oC for 18 h. The reaction mixture was concentrated under vacuum, and the residue was purified by a flash chromatograph on silica gel (hexane/ethyl acetate = 10/1) to give product **10** (243.5 mg) as colorless oil in 82% yield; R_f = 0.52 (silica gel, EtOAc/hexanes = 1/6); ^1H NMR (500 MHz, $CDCl_3$) δ = 4.74 (q, *J* = 6.3, 1H), 3.75 – 3.64 (m, 1H), 3.28 (t, *J* = 10.2, 1H), 2.31 (t, *J* = 12.2, 1H), 2.21 (s, 1H), 2.17 (d, *J* = 1.8, 2H), 1.87 (s, 1H), 1.77 (d, *J* = 12.7, 1H), 1.66 – 1.56 (m, 2H), 1.49 – 1.37 (m, 2H), 1.30 (d, *J* = 3.1, 1H), 1.26 (d, *J* = 6.5, 3H), 1.10 (s, 3H), 0.91 (d, *J* = 6.5, 3H), 0.85 (s, 9H), 0.63 – 0.52 (m, 1H), -0.01 (d, *J* = 31.7, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 206.27, 177.98, 141.34, 75.68, 63.35, 49.85, 49.27, 44.20, 44.10, 38.61, 35.10, 34.99, 32.27, 28.10, 25.99, 24.78, 22.64, 20.13, 18.29, -4.84, -4.94; HRMS (ESI) m/e 393.2815 [M+H^+] calcd for $C_{23}H_{41}O_3Si^+$: 393.2819.

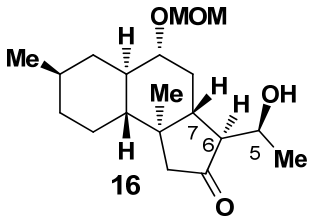
Synthesis of Compound 15:



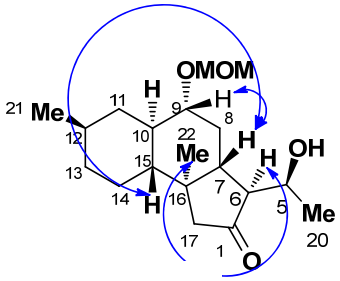
To a solution of alcohol **10** (500.0 mg, 1.27 mmol), DMAP (78.0 mg, 0.637 mmol) and DIPEA (329.0 mg, 2.55 mmol) in CH_2Cl_2 (6 mL) was added MOMCl (186.0 mg, 2.29 mmol) slowly at 0 ^oC, and then warmed to room temperature, and stirred for an additional 30 min. The reaction was quenched by addition of water (3 mL), and the mixture was extracted with ether (3 x 5 mL). The organic layers were washed with brine (3 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 10/1) to give a MOM ether (501.4 mg, 90%).

To a solution of the MOM ether (320.0 mg, 0.734 mmol) made above in CH_3CN (5 mL) was added HF (48 wt %, 3ml) slowly at 0 ^oC, and the resultant mixture was then warmed up to rt. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (5 mL), and the mixture was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine (3 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 4/1) to give **15** (189.0 mg, 80%); R_f = 0.36 (silica gel, EtOAc/hexanes = 1/2); ^1H NMR (500 MHz, $CDCl_3$) δ = 4.70 (t, *J* = 7.6, 1H), 4.57 (d, *J* = 2.8, 1H), 3.34 (d, *J* = 6.9, 3H), 3.22 – 3.11 (m, 2H), 2.21 (dd, *J* = 18.9, 7.7, 1H), 2.16 – 2.11 (m, 2H), 1.70 (d, *J* = 12.9, 1H), 1.57 – 1.47 (m, 2H), 1.32 (d, *J* = 6.7, 3H), 1.24 (dd, *J* = 12.6, 3.0, 1H), 1.21 – 1.18 (m, 1H), 1.06 (s, 3H), 0.88 (dd, *J*=11.7, 2.8, 1H), 0.85 (d, *J*=6.5, 3H), 0.49 (dd, *J*=24.0, 11.9, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.38, 176.27, 138.43, 96.08, 80.83, 77.26, 77.00, 76.75, 63.65, 55.52, 49.63, 48.93, 43.94, 42.19, 38.38, 34.72, 31.98, 31.46, 27.98, 23.62, 22.33, 19.99; HRMS (ESI) m/e 345.2023 [M+Na^+] calcd for $C_{19}H_{30}NaO_4^+$: 345.2036.

Synthesis of Compound 16:



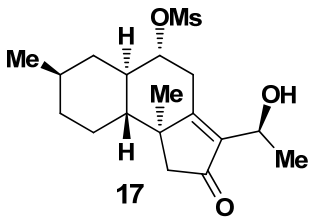
To a degassed solution of alcohol **15** (180.0 mg, 0.558 mmol) in EtOH (10 mL) and Na_2CO_3 (591.5 mg, 5.58 mmol) was added Pd/C (10%) (59.0 mg, 0.0558 mmol), and the mixture was purged with hydrogen, and then was stirred under a balloon of hydrogen for 8 h at rt. The reaction was worked by filtration of the reaction mixture then through a pad of Celite, and the filtrate was concentrated in vacuum. The residue was purified by a flash chromatography on silica gel. (hexane/ethyl acetate = 10/1) to give alcohol **16** (161.2 mg, 89%); R_f = 0.40 (silica gel, EtOAc/hexanes = 1/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.70 (t, *J* = 7.6, 1H), 4.62 – 4.48 (m, 2H), 3.34 (d, *J* = 6.9, 3H), 3.22 – 3.11 (m, 2H), 2.21 (dd, *J* = 18.9, 7.7, 1H), 2.16 – 2.11 (m, 2H), 1.70 (d, *J* = 12.9, 1H), 1.57 – 1.47 (m, 2H), 1.32 (d, *J* = 6.7, 3H), 1.24 (dd, *J* = 12.6, 3.0, 1H), 1.21 – 1.18 (m, 1H), 1.06 (s, 3H), 0.88 (dd, *J* = 11.7, 2.8, 1H), 0.85 (d, *J* = 6.5, 3H), 0.80 (dd, *J* = 7.0, 5.3, 1H), 0.49 (dd, *J* = 24.0, 11.9, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 220.69, 95.93, 81.13, 68.01, 55.98, 55.68, 53.42, 50.71, 46.38, 42.89, 40.15, 39.21, 34.97, 32.30, 30.74, 27.91, 22.77, 21.97, 14.99; HRMS (ESI) m/e 347.2214 [M+Na$^+$] calcd for $C_{19}H_{32}NaO_4^+$: 347.2193.



Carbon number	^{13}C-shift	^{1}H-shift
1	220.0	
5	67.8	3.83
6	55.8	2.04
7	46.3	1.62
8	35.0	2.21，1.50
9	81.3	3.24
10	42.7	1.50
11	39.0	0.61，2.16
12	32.2	1.34
13	34.8	1.71，0.89
14	27.8	1.22，1.51
15	50.6	1.01

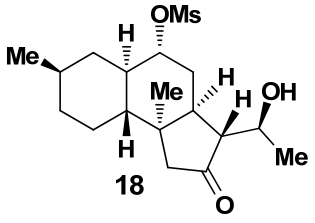
20	21.7	1.28
16	40.0	
17	53.3	2.19, 1.89
21	22.6	0.89
22	14.9	0.83

Synthesis of Compound 17:



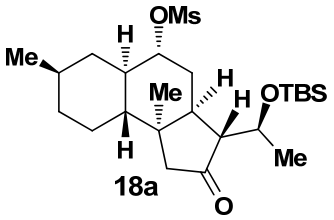
To a solution of alcohol **10** (2.20 g, 5.40 mmol), DMAP (660 mg, 5.40 mmol) and Et_3N (3.27 g, 32.4 mmol) in CH_2Cl_2 (30 mL) was added MsCl (1.86 g, 16.2 mmol) slowly at 0 ^oC, and the mixture then warmed up to rt, and then stirred for an additional 2h. The reaction was quenched by addition of water (15 mL), and the mixture was extracted with ether (3 x 15 mL), and the combined organic layers were washed with brine (5 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 10/1) to give a mesylate as a crude product, which was then dissolved in MeCN (20 mL). To this solution was added HF (48 wt %, 9 mL) at 0°C, and the resultant mixture was stirred at room temperature for 30 min. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (30 mL), and the mixture was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 4/1) to give alcohol **17** (1.30 g, 65% for two steps); R_f = 0.23 (silica gel, EtOAc/hexanes = 1/2); ^1H NMR (500 MHz, $CDCl_3$) δ = 4.72 – 4.58 (m, 1H), 4.29 – 4.19 (m, 1H), 3.45 (dd, *J* = 13.2, 5.2, 1H), 3.30 (d, *J* = 8.8, 1H), 3.05 (s, 3H), 2.61 – 2.49 (m, 1H), 2.28 – 2.17 (m, 2H), 2.10 – 2.05 (m, 1H), 1.82 – 1.71 (m, 2H), 1.71 – 1.57 (m, 2H), 1.38 (d, *J* = 6.7, 3H), 1.35 – 1.27 (m, 1H), 1.14 (s, 3H), 1.05 – 0.97 (m, 1H), 0.96 – 0.88 (m, 3H), 0.71 – 0.62 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 208.17, 173.12, 140.04, 83.79, 64.03, 49.75, 48.80, 43.97, 41.23, 38.65, 38.26, 34.61, 32.02, 31.92, 28.07, 24.06, 22.49, 20.28; HRMS (ESI) m/e 357.1730 [M+H^+] calcd for $C_{18}H_{29}O_5S^+$: 357.1730.

Synthesis of Compound 18:



To a degassed solution of alcohol **17** (1.05 g, 2.95 mmol) in EtOH (30 mL) and Et_3N (3.92 mL, 29.5 mmol) was added Pd/C (10%) (312 mg, 0.295 mmol), and the mixture was then purged with hydrogen, and then stirred under a balloon of hydrogen at rt for 8 h. The mixture was filtered through a pad of Celite, and the filtrate was concentrated in vacuum. The residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 10/1) to give alcohol **18** (0.74 g, 70%); R_f = 0.25 (silica gel, EtOAc/hexanes = 1/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.45 – 4.36 (m, 1H), 3.94 – 3.84 (m, 1H), 3.00 (s, 3H), 2.44 (d, *J* = 18.1, 1H), 2.40 – 2.31 (m, 1H), 2.24 (dd, *J* = 11.6, 5.4, 1H), 2.18 – 2.10 (m, 1H), 2.08 – 2.02 (m, 2H), 1.99 (d, *J* = 18.1, 1H), 1.76 – 1.71 (m, 1H), 1.63 – 1.54 (m, 2H), 1.37 – 1.32 (m, 1H), 1.31 (d, *J* = 6.4, 3H), 1.24 (s, 1H), 1.15 – 1.08 (m, 4H), 0.89 (d, *J* = 6.6, 3H), 0.88 – 0.78 (m, 2H), 0.68 – 0.58 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 219.42, 83.17, 68.41, 54.95, 51.98, 46.50, 43.81, 41.46, 38.82, 38.79, 38.39, 34.81, 31.92, 29.95, 27.08, 22.50, 21.28, 20.47; HRMS (ESI) m/e 359.1885 [M+H$^+$] calcd for $C_{18}H_{31}O_5S^+$: 359.1887.

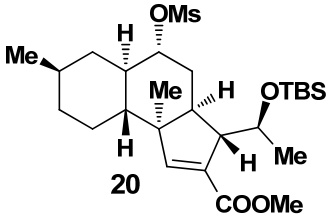
Synthesis of Compound 18a:



18a

To a solution of the crude alcohol **18** (591.0 mg, 1.65 mmol) and Et_3N (333 mg, 3.30 mmol) in dry CH_2Cl_2 (10 mL) was added TBSOTf (436 mg, 1.65 mmol) at -78 ^{o}C in a dropwise manner, and the reaction mixture was stirred at -78 ^{o}C for 0.5h. The reaction was quenched with water (2 mL), and the mixture was extracted with ether (3 x 5 mL). The combined organic layers were washed with brine (3 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel. (hexane:ethyl acetate = 4:1) to give silylether **18a** (701.3 mg, 90%); R_f = 0.85 (silica gel, EtOAc/hexanes = 1/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.40 – 4.31 (m, 1H), 4.00 (d, *J* = 4.7, 1H), 3.00 (s, 3H), 2.38 – 2.31 (m, 2H), 2.29 – 2.20 (m, 1H), 2.10 (d, *J* = 10.7, 1H), 2.07 – 1.97 (m, 2H), 1.93 (d, *J* = 17.0, 1H), 1.72 (d, *J* = 12.8, 1H), 1.62 – 1.54 (m, 2H), 1.31 (d, *J* = 6.3, 4H), 1.09 (s, 4H), 0.88 (d, *J* = 6.5, 3H), 0.85 (s, 9H), 0.83 – 0.78 (m, 2H), 0.61 (q, *J*=12.0, 1H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 216.50, 83.80, 68.24, 55.38, 53.22, 45.95, 43.58, 41.21, 38.94, 38.53 , 38.39, 34.77, 31.94, 29.77, 26.98, 26.04, 22.55, 21.51, 20.52, 18.15, -4.15, -4.72; HRMS (ESI) m/e 473.2759 [M+H$^+$] calcd for $C_{24}H_{45}O_5SSi^+$: 473.2751.

Synthesis of Compound 20:

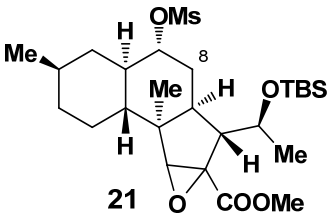


20

To a stirred solution of ketone **18a** (780.0 mg, 1.65 mmol) in THF (5 mL) at –78 °C was added KHMDS (1.0 M in THF, 3.30 mmol, 3.30 mL), and the resultant mixture was then stirred at

the same temperature for 1 h. To this solution was added a solution of Commins' reagent (966.0 mg, 2.47 mmol) in THF (2 mL), and the resultant mixture was stirred at –78 °C for 1 h. The reaction mixture was quenched by addition of a saturated solution of NH_4Cl (6 mL), and the mixture was extracted with Et_2O (3 x 5 mL). The combined organic layers were washed with brine (2 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 20/1) to give a triflate (270 mg, 0.446 mmol), which was then dissolved in a mixed solvent of DMF/MeOH (12 mL, 1/3). To this solution was added Et_3N (0.18 mL, 1.34 mmol) and $Pd(PPh_3)_4$ (106.0 mg, 0.0892 mmol), and the resultant mixture was heated to 50 ^oC, and stirred for 12 h under a CO atmosphere (1 atm). The reaction was quenched by addition of a saturated solution of NH_4Cl (10 mL), and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 10/1) to give product **20** (149.4 mg) in 65% yield; R_f = 0.62 (silica gel, EtOAc/hexanes = 1/4); ^1H NMR (500 MHz, $CDCl_3$) δ = 6.70 (s, 1H), 4.57 (d, *J*=6.1, 1H), 4.40 (d, *J* = 5.6, 1H), 3.68 (s, 3H), 2.98 (s, 3H), 2.76 (d, *J* = 8.1, 1H), 2.44 (d, *J*=7.1, 1H), 2.19 (d, *J* = 14.0, 1H), 2.02 (d, *J*=12.0, 1H), 1.94 – 1.85 (m, 1H), 1.69 (d, *J* = 12.7, 1H), 1.59 (d, *J* = 11.1, 1H), 1.51 (d, *J* = 11.3, 1H), 1.31 (s, 1H), 1.24 (t, *J* = 10.9, 2H), 1.19 (d, *J* = 6.3, 3H), 1.07 (s, 3H), 0.96 (t, *J* = 10.9, 1H), 0.86 (d, *J* = 6.2, 3H), 0.79 (s, 9H), 0.69 – 0.59 (m, 1H), -0.07 (d, *J* = 48.0, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 166.16, 152.79, 134.82, 85.06, 66.43, 55.14, 51.25, 48.23, 46.58, 42.80, 40.60, 39.42, 38.77, 34.92, 32.66, 32.01, 27.70, 25.89, 22.79, 22.54, 19.41, 18.12, -4.01, -5.15; HRMS (ESI) m/e 515.2850 [$M+H^+$] calcd for $C_{26}H_{47}O_6SSi^+$: 515.2857.

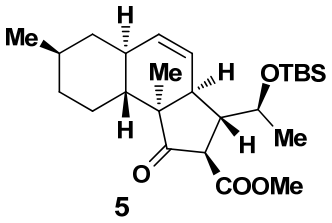
Synthesis of Compound 21:



To a mixture of *m*-CPBA (283.0 mg, 1.63 mmol) and $NaHCO_3$ (68.5 mg, 0.816mmol) in dry $ClCH_2CH_2Cl$ (6 mL), was added a solution of α,β -unsaturated methyl ester **20** (210.0 mg, 0.408 mmol) in dry $ClCH_2CH_2Cl$ (2 mL) under argon at room temperature, and the resultant mixture was heated to 45 ^oC, and then stirred for 12 h, the reaction mixture was quenched by addition of a saturated solution of $NaHSO_3$ (5 mL). The mixture was extracted with Et_2O (3 x 5 mL), and the combined organic layers were washed with brine (2 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 15/1) to give product **21** (162.4 mg) in 75% yield; R_f= 0.46 (silica gel, EtOAc/hexanes = 1/4); ^1H NMR (500 MHz, $CDCl_3$) δ = 4.41 – 4.33 (m, 1H), 4.04 – 3.96 (m, 1H), 3.76 (s, 3H), 3.35 (s, 1H), 2.99 (s, 3H), 2.59 – 2.53 (m, 1H), 2.30 – 2.24 (m, 1H), 2.05 (d, *J* = 1.9, 1H), 1.75 – 1.67 (m, 3H), 1.57 – 1.51 (m, 1H), 1.46 (d, *J* = 3.4, 1H), 1.24 (d, *J* = 5.1, 1H), 1.21 (d, *J* = 6.3, 3H), 1.12 – 1.08 (m, 1H), 1.05 (s, 3H), 0.92 – 0.89 (m, 4H), 0.88 (s, 9H), 0.85 (s, 2H), 0.76 – 0.68 (m, 1H), 0.05 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.41, 83.90, 68.45, 67.56, 62.12, 52.47, 48.09, 42.85, 42.62, 42.32, 40.89, 38.88, 38.21, 34.64, 31.72, 29.84, 27.56, 26.03,

22.55, 21.64, 18.18, 15.80, -4.67, -4.70; HRMS (ESI) m/e 531.2802 [M+H$^+$] calcd for $C_{26}H_{47}O_7SSi^+$: 531.2806.

Synthesis of Compound 5:



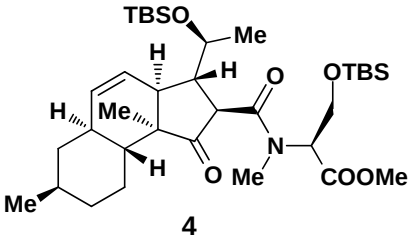
5

To a solution of **21** (67.0 mg, 0.13 mmol) in PhMe (3 mL) was added DBU at rt, and the resultant mixture was stirred at 120 ^oC for 48 h. The reaction was quenched by addition of a saturated solution of NH_4Cl (5 mL), and the mixture was extracted with Et_2O (3 x 5 mL). The combined extracts were dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash column chromatography on silica gel to give a olefin as a crude product.

To a solution of the above residue in THF-H_2O (5 mL, 9/1) was deoxygenated with Ar for 10 min, followed by addition of SmI_2 (0.1 M in THF, 2.5 mL, 0.25 mmol). The resultant mixture was stirred at rt under Ar for 1h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (5 mL), and the mixture was extracted with Et_2O (3 x 5 mL). The combined organic layers were washed with brine (3 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 10/1) to give an alcohol (40.0 mg, 0.092 mmol), which was then dissolved in CH_2Cl_2 (4 mL).

To this solution was added DMP (77.0 mg, 0.183mmol) at rt under N_2, and the resultant mixture was stirred at rt for 1.5 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (5 mL), and the mixture was then extracted with Et_2O (3 x 5 mL). The combined organic layers were washed with brine (2 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate =25/1) to give product **5** (25.2 mg) in 46% yield for three steps. R_f = 0.86 (silica gel, EtOAc/hexanes = 1/8); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.64 (d, *J* = 9.7, 1H), 5.41 (d, *J* = 10.0, 1H), 4.13 (d, *J* = 3.9, 1H), 4.00 (d, *J* = 4.2, 1H), 3.69 (s, 3H), 2.69 – 2.57 (m, 1H), 2.32 – 2.19 (m, 2H), 2.12 (d, *J* = 10.1, 1H), 1.76 (d, *J* = 11.3, 3H), 1.66 (d, *J* = 10.9, 2H), 1.42 (s, 1H), 1.25 (s, 1H), 1.22 (d, *J* = 6.3, 3H), 1.12 (t, *J* = 10.0, 1H), 0.89 (s, 15H), 0.75 – 0.66 (m, 1H), 0.07 (d, *J* = 6.2, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 174.94, 132.12, 127.54, 81.28, 69.10, 55.01, 52.86, 51.93, 47.18, 46.00, 45.30, 42.31, 37.19, 35.89, 33.11, 29.84, 26.07, 25.85, 22.60, 21.40, 18.28, 15.37, -4.25, -4.50; HRMS (ESI) m/e 435.2923 [M+H$^+$] calcd for $C_{25}H_{43}O_4Si^+$: 435.2925.

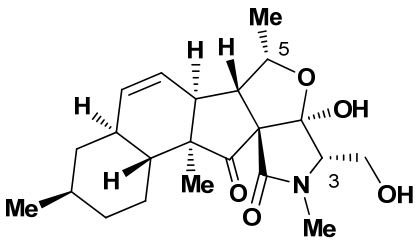
Synthesis of Compound 4:



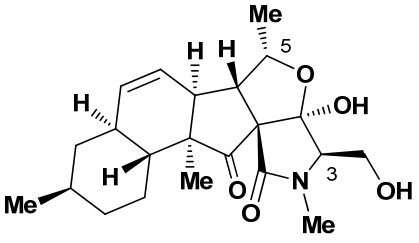
4

To a stirred solution of **5** (20.0 mg, 0.046 mmol) and DMAP (29 mg, 0.23 mmol) in toluene (1 mL) was added **7** (113.0 mg, 0.46 mmol) at room temperature, and the mixture was heated to 90 °C, and then stirred for 30 h. The reaction mixture was concentrated under vacuum, and the residue was purified by a flash chromatography on silica gel (hexane/ethyl acetate = 20/1) to give product **4** (21.8 mg, 73%). R_f = 0.55 (silica gel, EtOAc/hexanes = 1/8); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.91 – 5.82 (m, 1H), 5.46 (t, *J* = 8.5, 1H), 5.00 – 4.91 (m, 1H), 4.17 – 4.06 (m, 1H), 4.04 – 3.95 (m, 1H), 3.92 – 3.84 (m, 1H), 3.66 (s, 3H), 3.32 (s, 3H), 2.90 – 2.79 (m, 1H), 2.60 – 2.42 (m, 1H), 2.41 – 2.32 (m, 1H), 1.77 (d, *J* = 4.3, 2H), 1.66 (d,*J* = 13.6, 1H), 1.61 – 1.56 (m, 1H), 1.52 – 1.46 (m, 1H), 1.43 – 1.36 (m, 2H), 1.34 – 1.30 (m, 2H), 1.28 (s, 2H), 1.25 (s, 3H), 1.23 (d, *J* = 6.4, 3H), 1.20 – 1.15 (m, 1H), 0.88 (d, *J* = 7.9, 18H), 0.08 – 0.04 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ = 213.83 (s), 169.70 (s), 168.81 (s), 131.27 (s), 127.18 (s), 69.48 (s), 62.19 (s), 60.42 (s), 55.40 (s), 52.84 (s), 51.75 (s), 51.30 (s), 44.55 (s), 41.68 (s), 37.94 (s), 36.58 (s), 35.28 (s), 34.84 (s), 32.93 (s), 29.66 (s), 25.88 (s), 25.72 (s), 25.31 (s), 23.20 (s), 22.25 (s), 18.05 (s), 15.15 (s), -3.89 (s), -4.88 (s), -5.62 (s), -5.71 (s); HRMS (ESI) m/e 650.4275 [M+H$^+$] calcd for $C_{35}H_{63}NO_6Si_2^+$: 650.4267.

Syntheses of Compound 1 and 22:



(+)-fusarisetin A (**1**)



C3-*epi*-(+)-fusarisetin A (**22**)

To a solution of disilylether **4** (9.0 mg, 0.0138 mmol) in AcOH/THF/H_2O (2.5 mL, 3:1:1) was added HF (1ml, 48 wt %) slowly at 0 °C, and the mixture was then warmed up to rt, and stirred for an additional 30 min. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ (5 mL), and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine (2 mL), and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified chromatography on silica gel (CH_2Cl_2/acetone, from 10/1 to 4/1) to give a diol (5.0 mg, 0.012 mmol, 86%), which was then dissolved in dry MeOH. To this solution was added NaOMe (0.5 M in MeOH, 0.12 ml, 0.06 mmol) slowly at 0 °C, and the mixture was stirred at the same temperature for 10 min. After stirring at room temperature for 1 h, the reaction was quenched by addition of a saturated solution of NH_4Cl (0.5 mL), and mixture was extracted EA (3 x 5 mL). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by a flash chromatography on silica gel (CH_2Cl_2/acetone from 10/1 to 4/1) to give (+)-fusarisetin A (**1**) (2.0 mg, 43%); and C3-epi-(+)-fusarisetin A (**22**) (1.4 mg, 30%).

R_f (+)-fusarisetin A (**1**) = 0.28 (silica gel, CH_2Cl_2/acetone = 1/4).

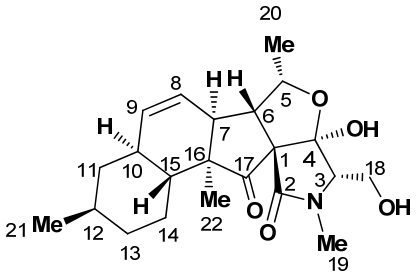
^{1}H NMR (500 MHz, MeOD) δ = 5.85 – 5.75 (m, 1H), 5.57 (d, *J* = 9.9, 1H), 4.35 (q, *J* = 12.5, 6.3, 1H), 3.90 – 3.81 (m, 2H), 3.59 (t, *J* = 5.0, 1H), 2.87 – 2.81 (m, 1H), 2.68 (dd, *J* = 10.9, 4.6, 1H), 1.88 (d, *J* = 13.1, 2H), 1.75 (d, *J* = 12.8, 1H), 1.58 – 1.48 (m, 3H), 1.46 (d, *J* = 6.5, 3H), 1.14 – 1.07 (m, 1H), 0.98 (d, *J* = 7.9, 4H), 0.93 (t, *J* = 5.9, 3H), 0.84 (d, *J* = 11.9, 1H). ^{13}C NMR (126 MHz, MeOD) δ = 214.11, 172.08, 133.63, 126.90, 109.69, 79.65, 76.47, 71.67, 61.81, 56.38,

55.34, 44.69, 43.30, 39.06, 38.02, 34.33, 29.93, 26.58, 22.92, 17.81, 14.36; HRMS (ESI) m/e 412.2089 [M+Na$^+$] calcd for $C_{22}H_{31}NNaO_5^+$: 412.2079.

R_f (C3-epi-(+)-fusarisetin A (**22**) = 0.20 (silica gel, CH_2Cl_2/acetone = 1/4).

^{1}H NMR (500 MHz, MeOD) δ = 5.79 (s, 1H), 5.55 (d, *J* = 9.9, 1H), 4.35 – 4.25 (m, 1H), 4.00 – 3.93 (m, 1H), 3.79 – 3.71 (m, 1H), 3.68 – 3.59 (m, 1H), 2.97 (s, 3H), 2.82 – 2.73 (m, 1H), 2.64 (d, *J* = 10.8, 1H), 1.86 (d, *J* = 13.5, 2H), 1.74 (d, *J* = 11.3, 1H), 1.57 (d, *J* = 12.6, 1H), 1.51 – 1.44 (m, 2H), 1.43 (d, *J* = 6.4, 3H), 1.09 (dd, *J* = 20.7, 8.5, 1H), 0.98 (d, *J* = 6.9, 4H), 0.92 (d, *J* = 6.5, 3H), 0.85 – 0.78 (m, 1H). ^{13}C NMR (101 MHz, MeOD) δ = 213.47, 172.38, 133.51, 126.82, 109.73, 79.74, 76.75, 70.82, 60.42, 55.59, 54.86, 44.47, 43.21, 39.13, 37.90, 36.40, 34.22, 28.86, 26.45, 22.81, 17.42, 14.09; HRMS (ESI) m/e 412.2089 [M+Na$^+$] calcd for $C_{22}H_{31}NNaO_5^+$: 412.2079.

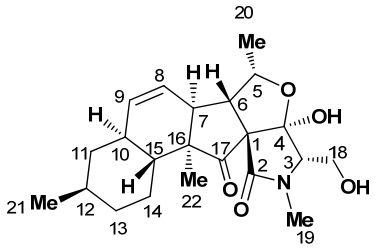
Table S1: ^{1}H NMR (CD_3OD) spectroscopic data comparison of natural and synthetic fusarisetin A.



Position	Natural δ ^{1}H [ppm, mult, J(Hz)] 800 MHz	Synthetic δ ^{1}H [ppm, mult, J (Hz)] 500 MHz	Err (Natural–Synthetic) Δδ (ppm)
1			
2			
3	3.60 (dd, 5.0, 2.5)	3.59 (t, 5.0)	0.01
4			
5	4.37 (q, 6.3)	4.35 (m)	0.02
6	2.87 (dd, 11.0, 5.8)	2.86 (m)	0.01
7	2.69 (dd, 11.0, 4.8)	2.68 (dd, 10.9, 4.6)	0.01
8	5.83 (ddd, 2.5, 4.8, 10.0)	5.82 (m)	0.01
9	5.58 (d, 10.0)	5.57 (d, 9.9)	0.01
10	1.90 (m)	1.89 (m)	0.01
11	1.87 (m) 0.85 (dq, 12.8)	1.89 (m) 0.84 (q, 12.8)	-0.02 0.01
12	1.51 (m)	1.54 (m)	-0.03
13	1.76 (br d, 12.8) 0.99 (m)	1.75 (d, 12.8) 0.99 (m)	0.01 0.00
14	1.56 (m) 1.13 (ddd, 12.8, 9.6, 3.2)	1.54 (m) 1.12(dd, 24.9, 12.6)	0.02 0.01
15	1.53 (m)	1.54 (m)	-0.01
16			
17			
18	3.89 (dd, 12.0, 5.0)	3.89 (dd, 12.1, 5.1)	0.00

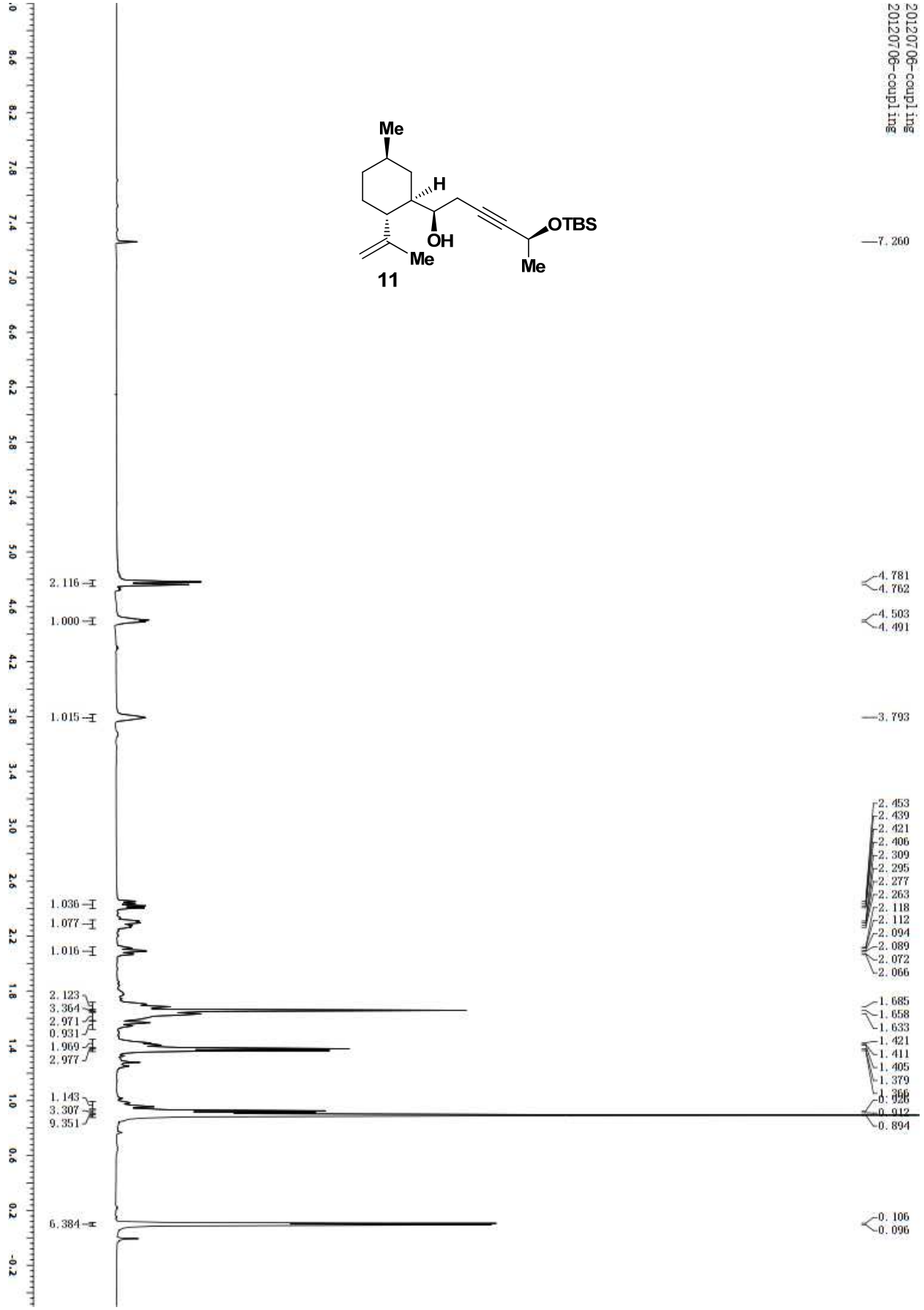
	3.84 (dd, 12.0, 5.0)	3.83 (dd, 12.0, 5.1)	0.01
19	2.97 (s)	2.97 (s)	0.00
20	1.47 (d, 6.5)	1.46 (d, 6.5)	0.01
21	0.94 (d, 6.5)	0.93 (d, 5.9)	0.01
22	0.98 (s)	0.98 (s)	0.00

Table S2. ^{13}C NMR (CD_3OD) spectroscopic data comparison of natural and synthetic fusarisetin A.

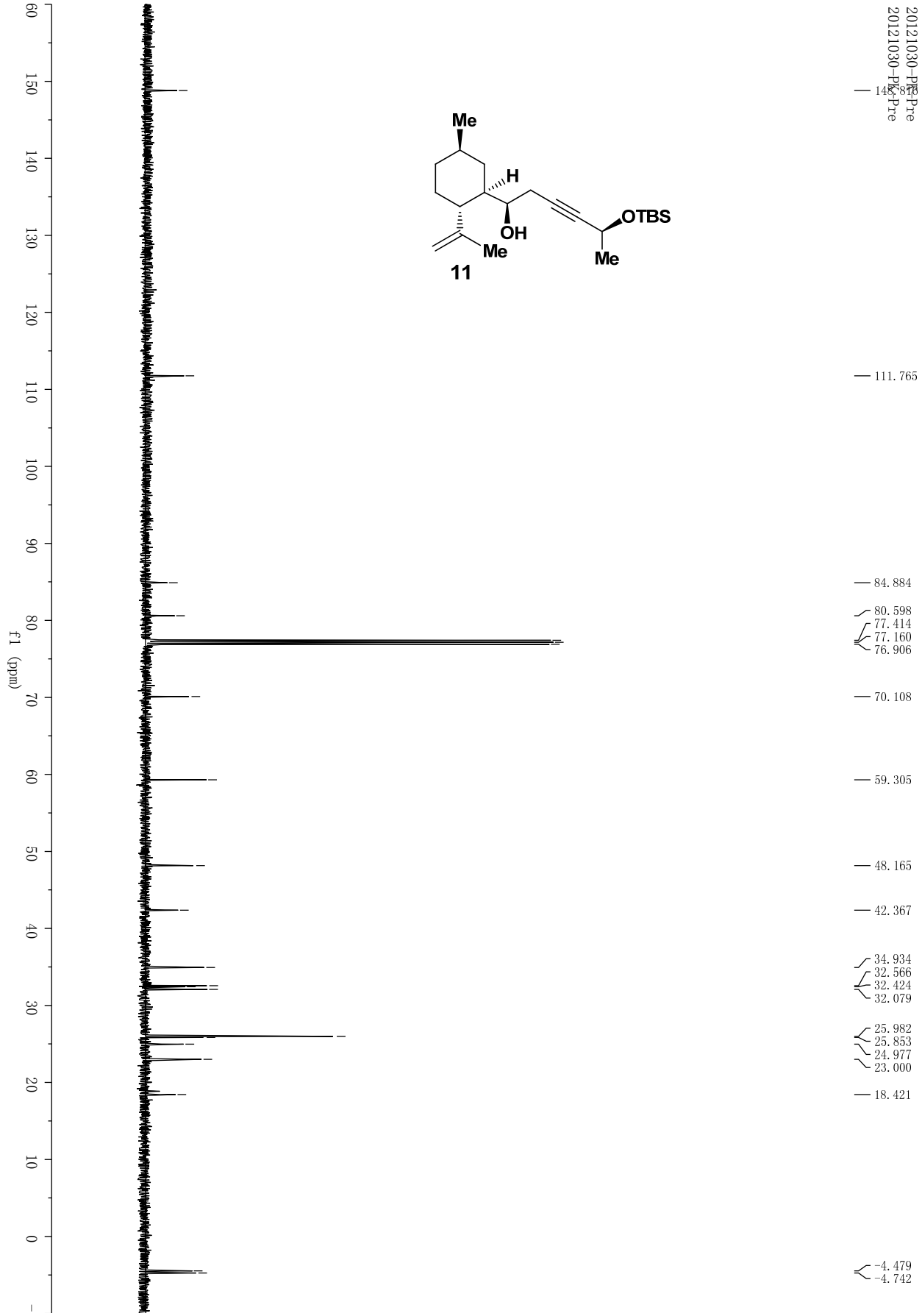


Position	Natural δ ^{13}C (ppm) 200 MHz	Synthetic δ ^{13}C (ppm) 126 MHz	Err (Synthetic–Natural) Δδ (ppm)
1	75.3	76.30	1.00
2	170.9	171.91	1.01
3	70.5	71.50	1.00
4	108.5	109.52	1.02
5	78.5	79.48	0.98
6	54.2	55.17	0.97
7	43.5	44.51	1.01
8	125.7	126.72	1.02
9	132.5	133.46	0.96
10	36.8	37.85	1.05
11	42.1	43.13	1.03
12	33.1	34.16	1.06
13	35.3	36.33	1.03
14	25.4	26.41	1.01
15	37.9	38.89	0.99
16	55.2	56.21	1.01
17	212.9	213.94	1.04
18	60.6	61.64	1.04
19	28.8	29.76	0.96
20	16.6	17.64	1.04
21	21.7	22.75	1.05
22	13.2	14.19	0.99

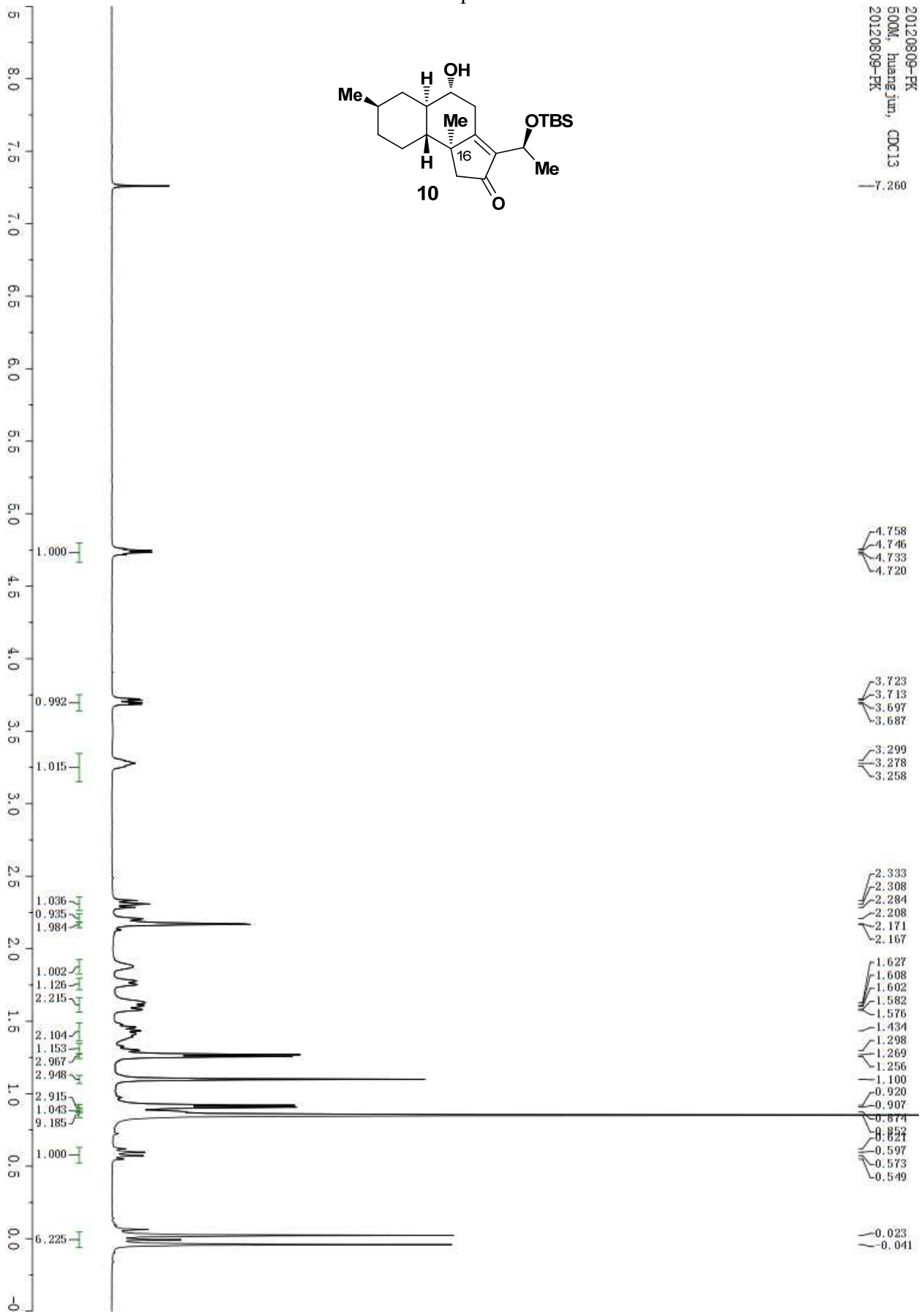
^{1}H NMR Spectra of **11**



^{13}C NMR Spectra of **11**

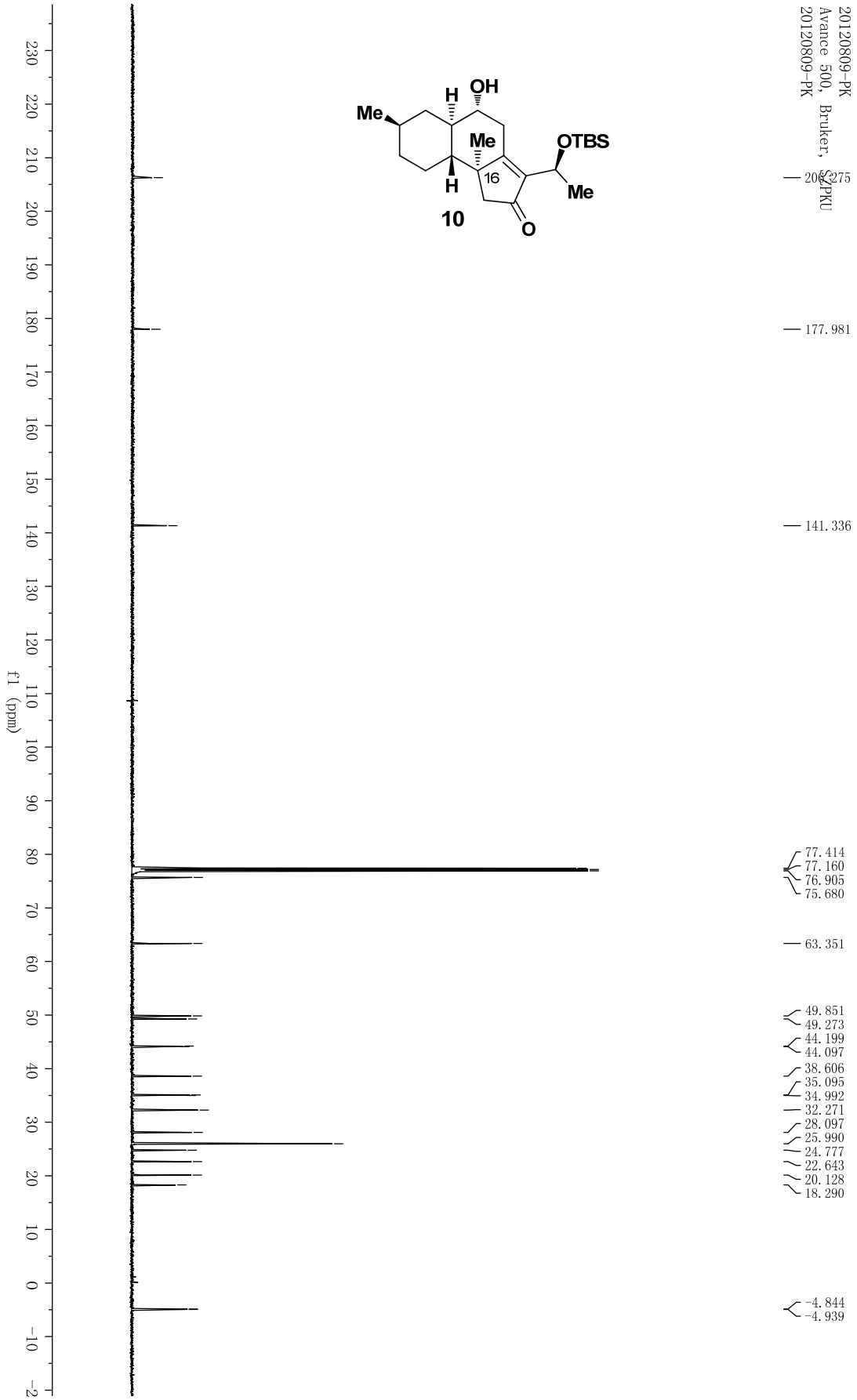


^{1} H NMR Spectra of **10**

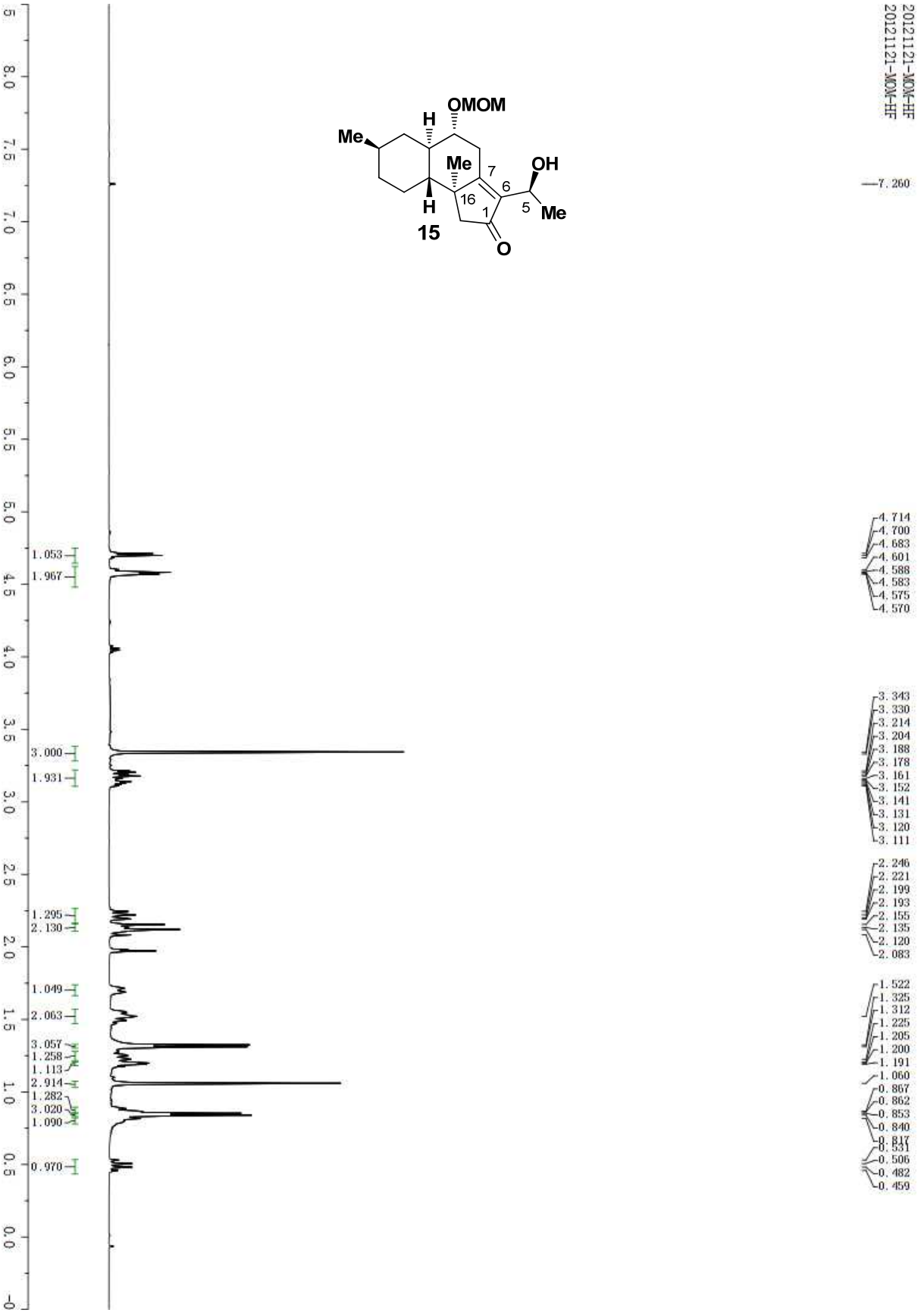


10

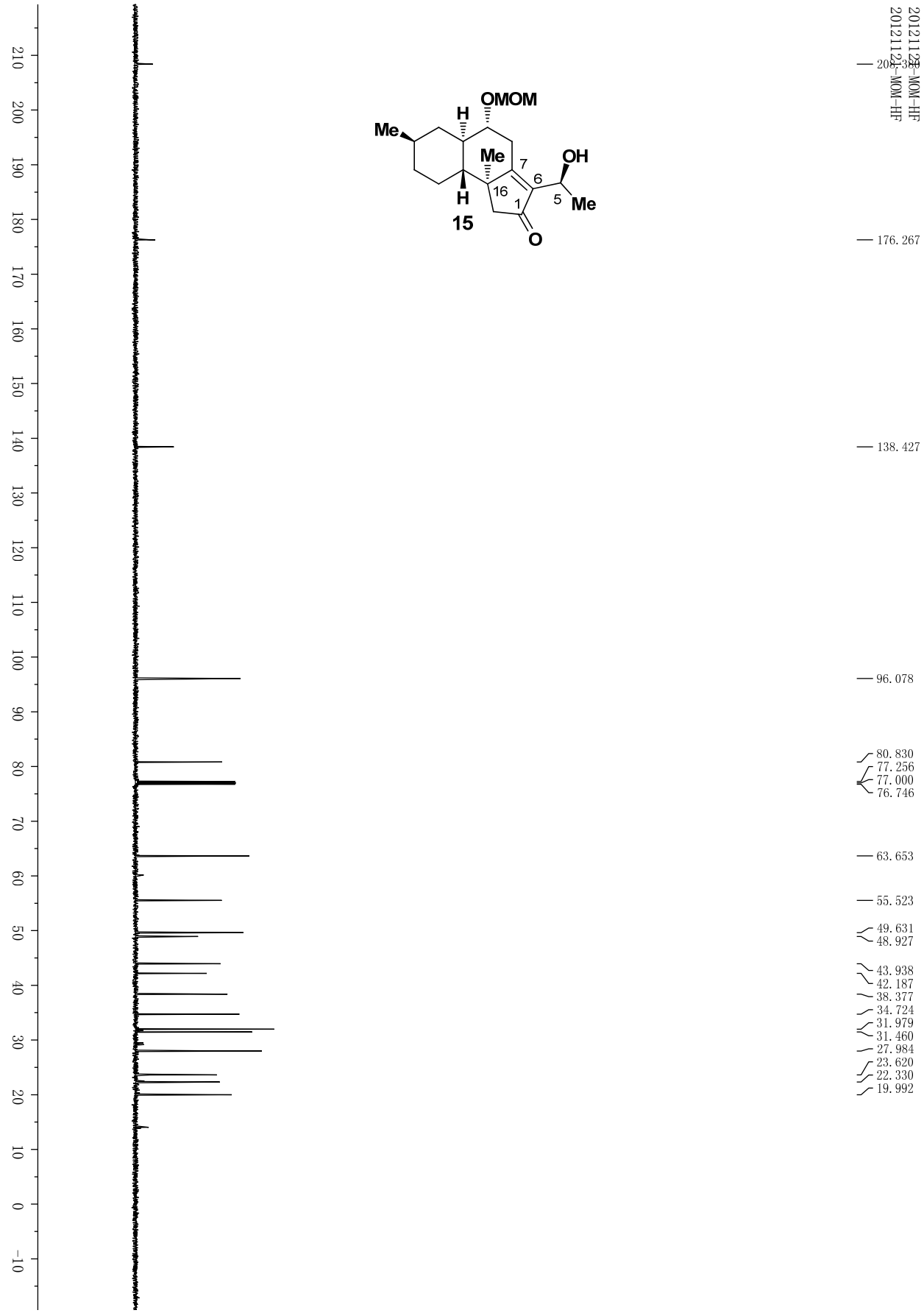
^{13} C NMR Spectra of **10**



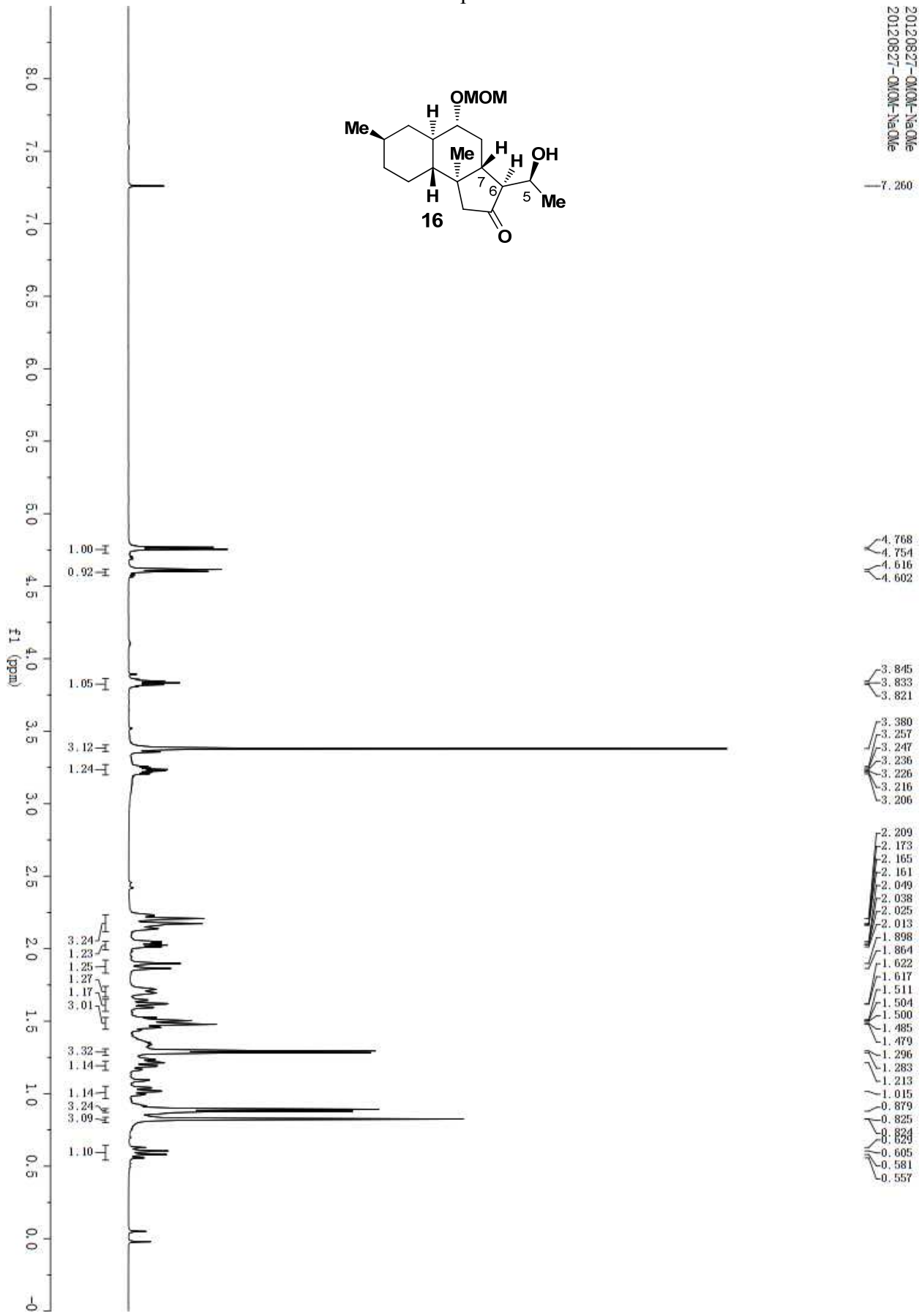
[1] H NMR Spectra of **15**



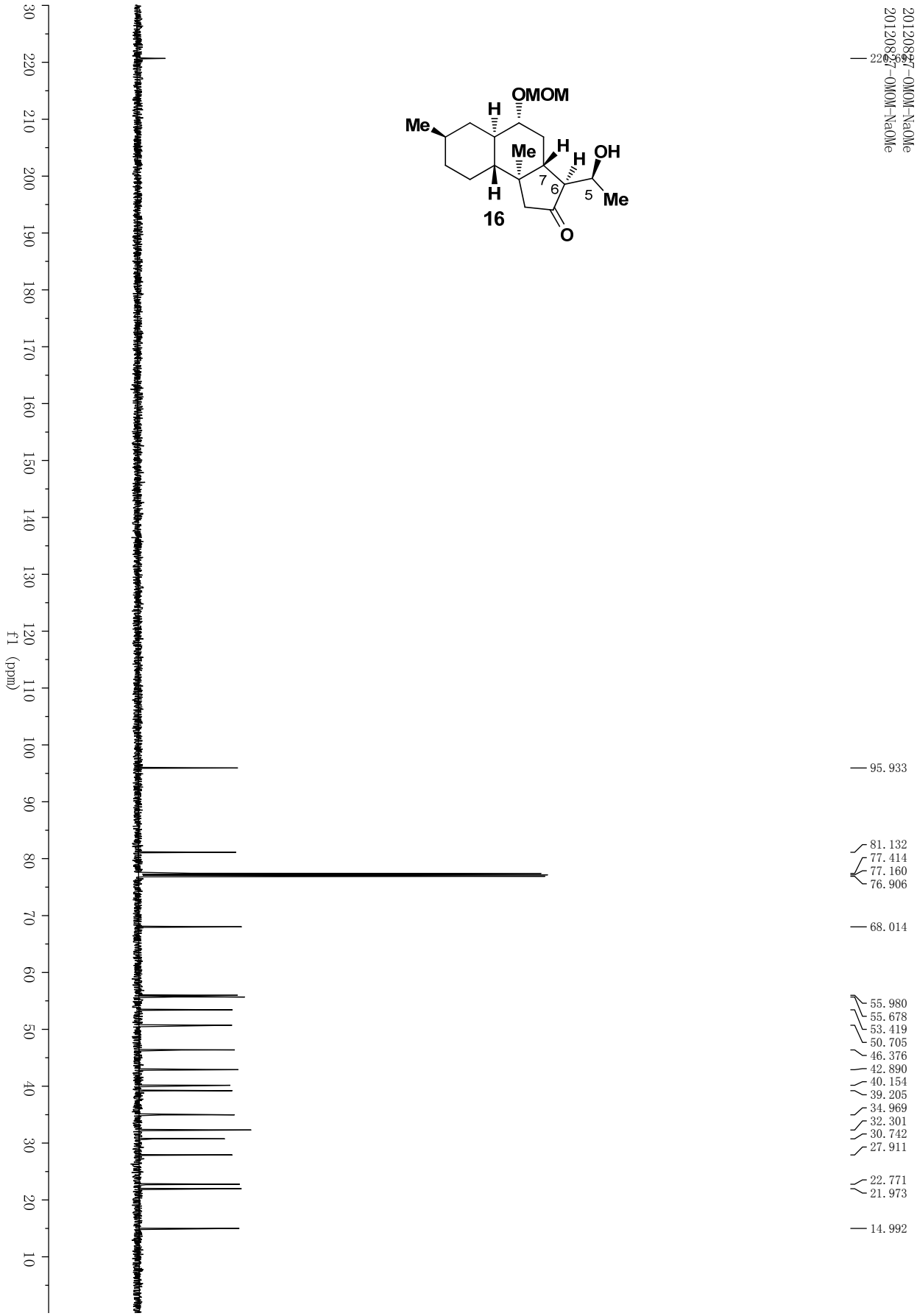
^{13}C NMR Spectra of **15**



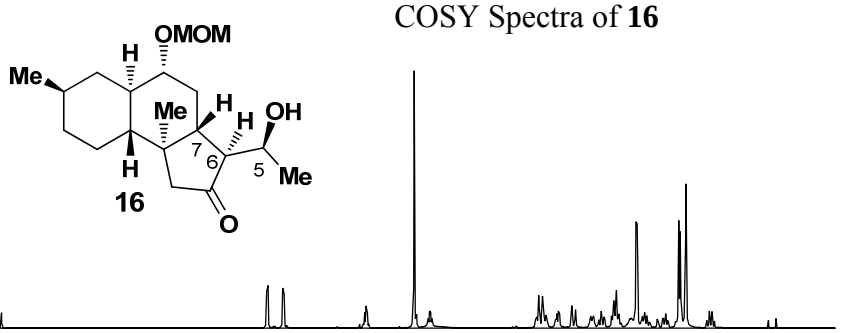
^{1}H NMR Spectra of **16**

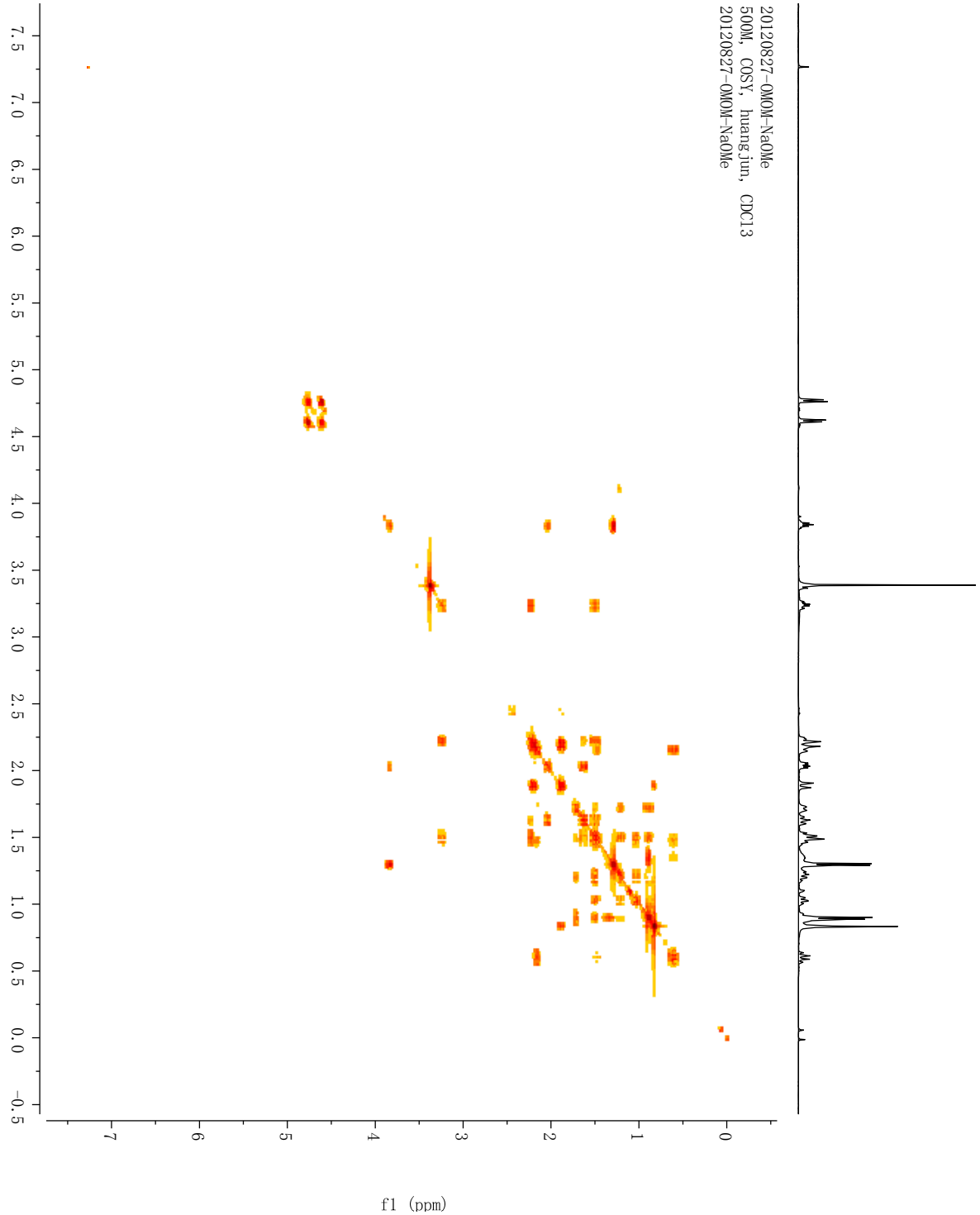


^{13} C NMR Spectra of **16**

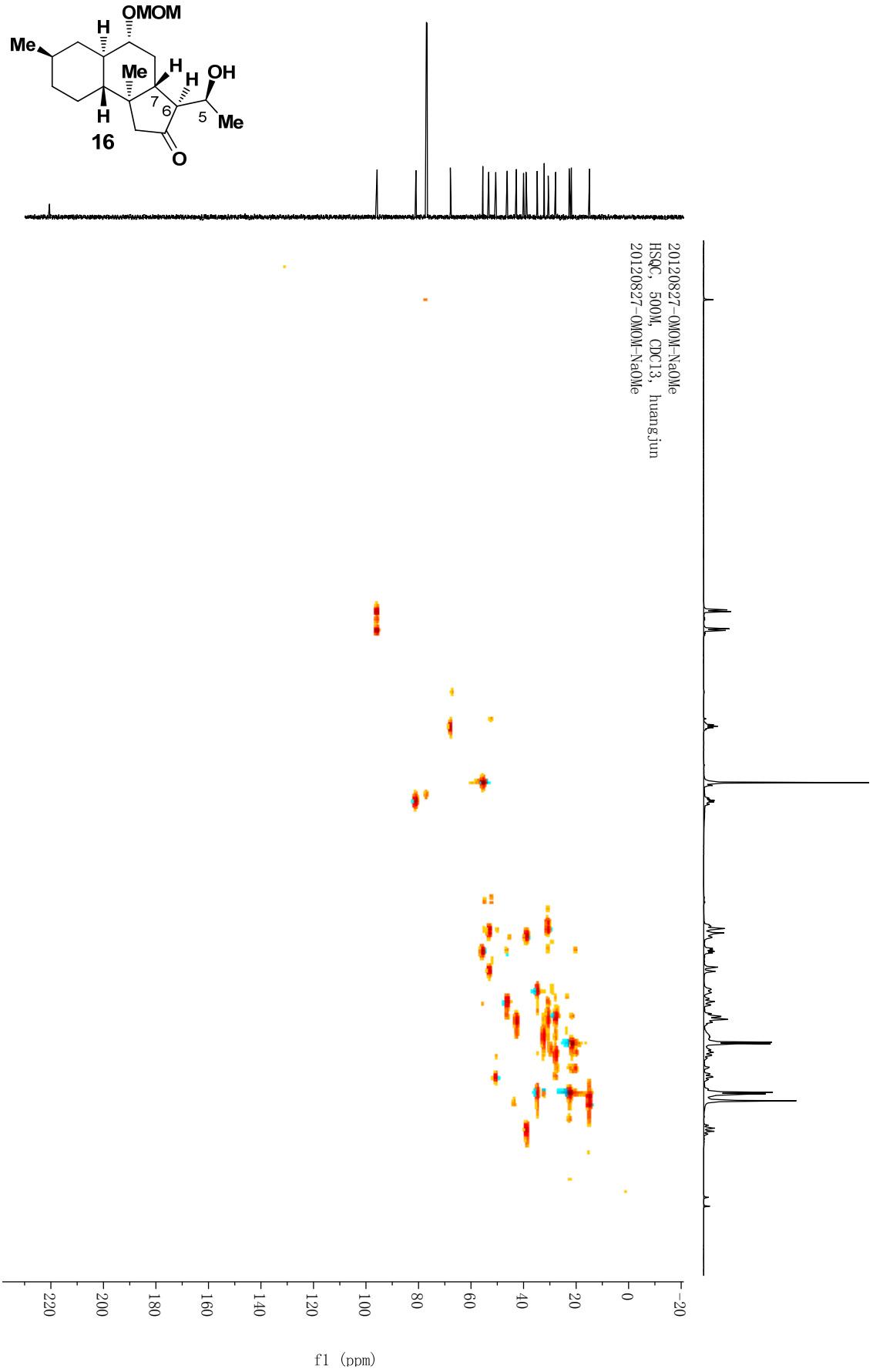


COSY Spectra of **16**

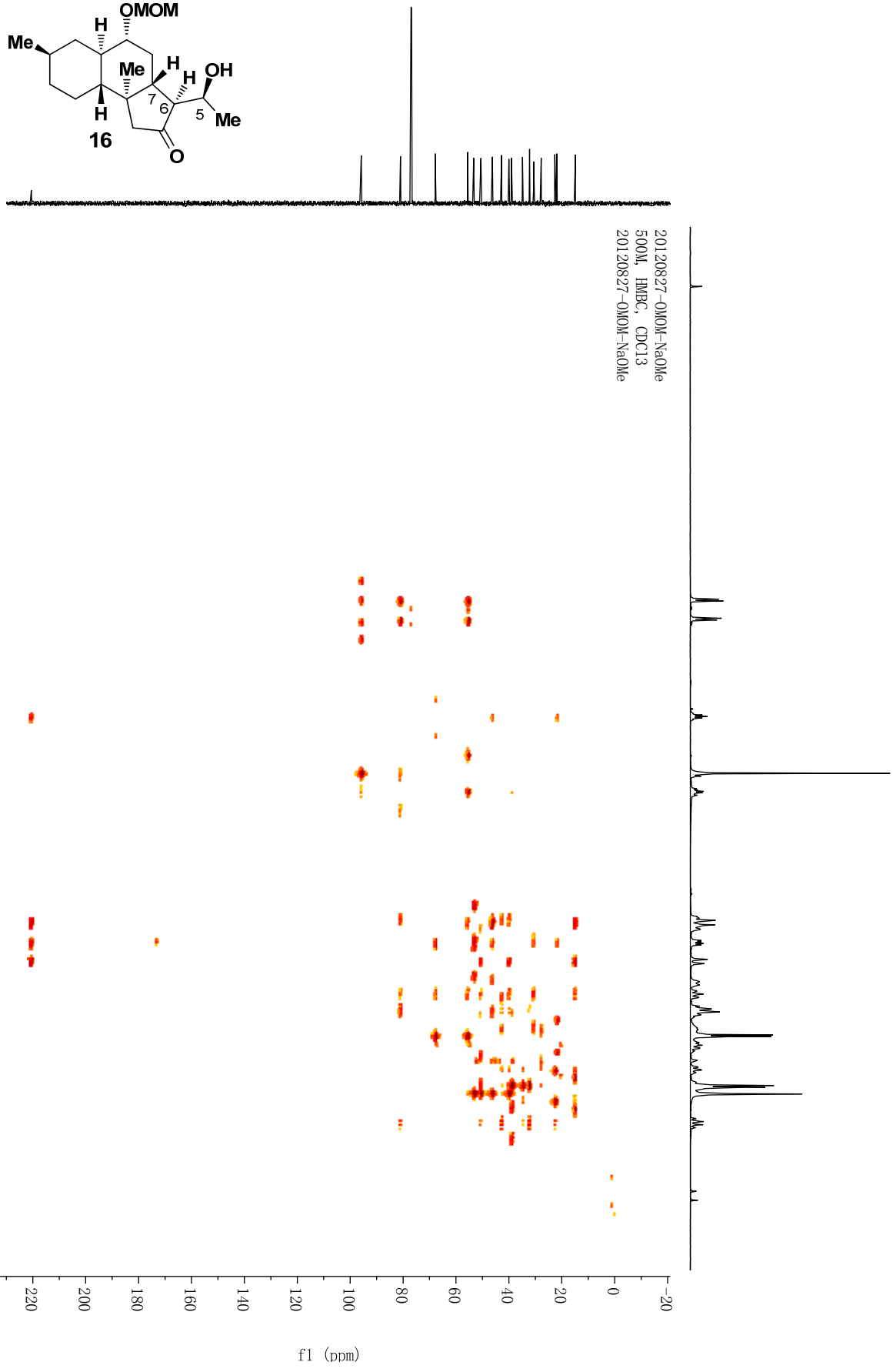




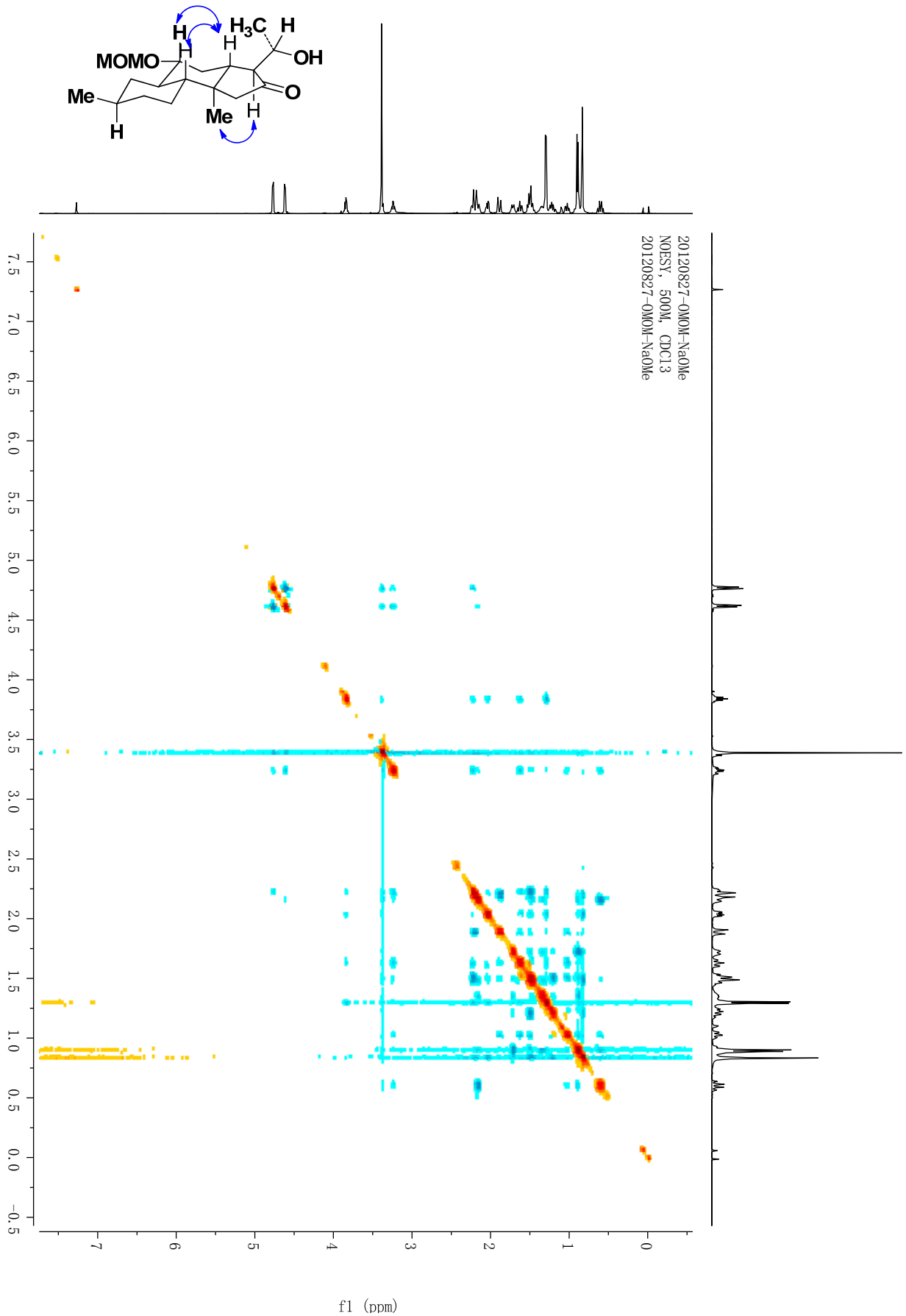
HSQC Spectra of **16**



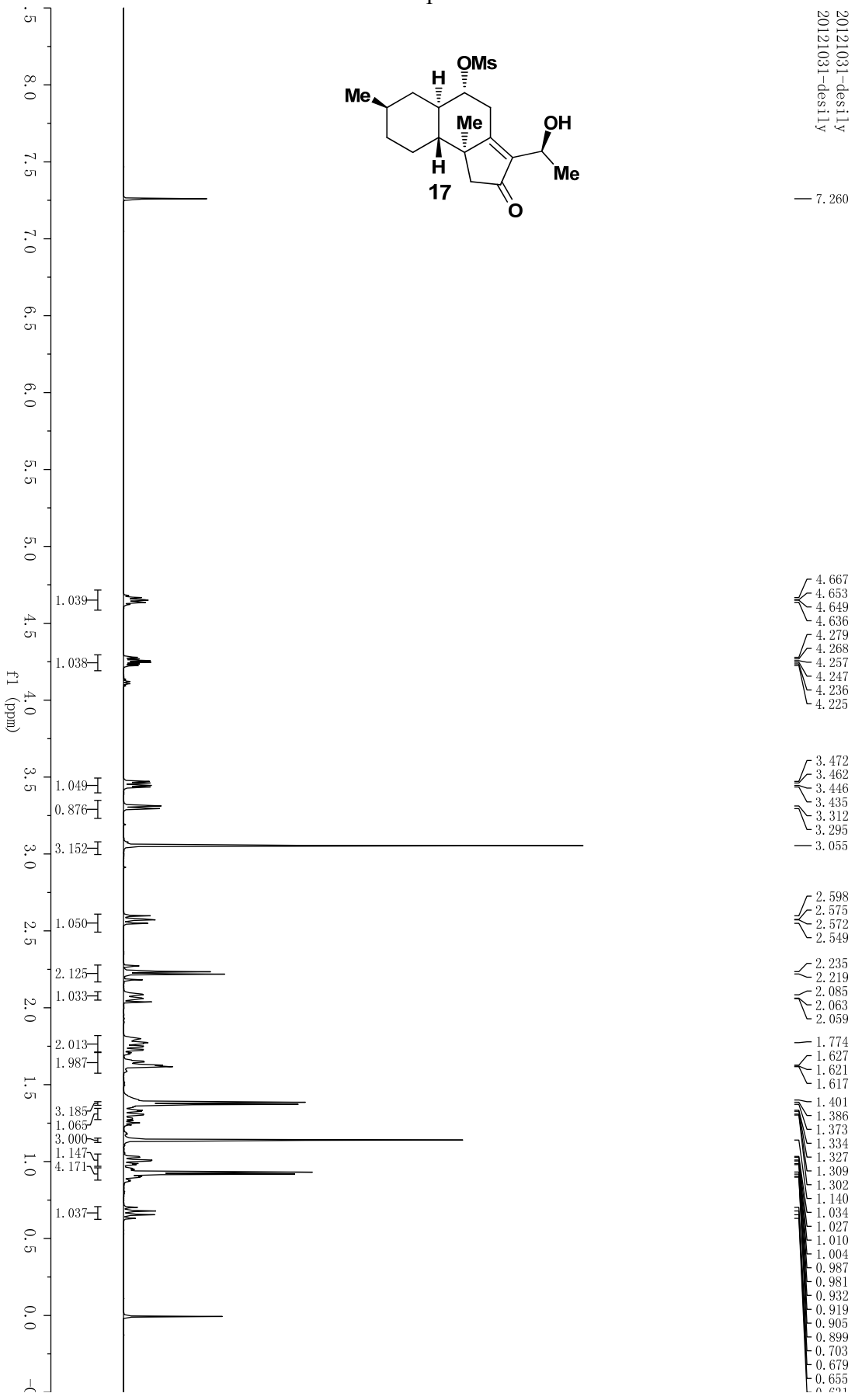
HMBC Spectra of **16**



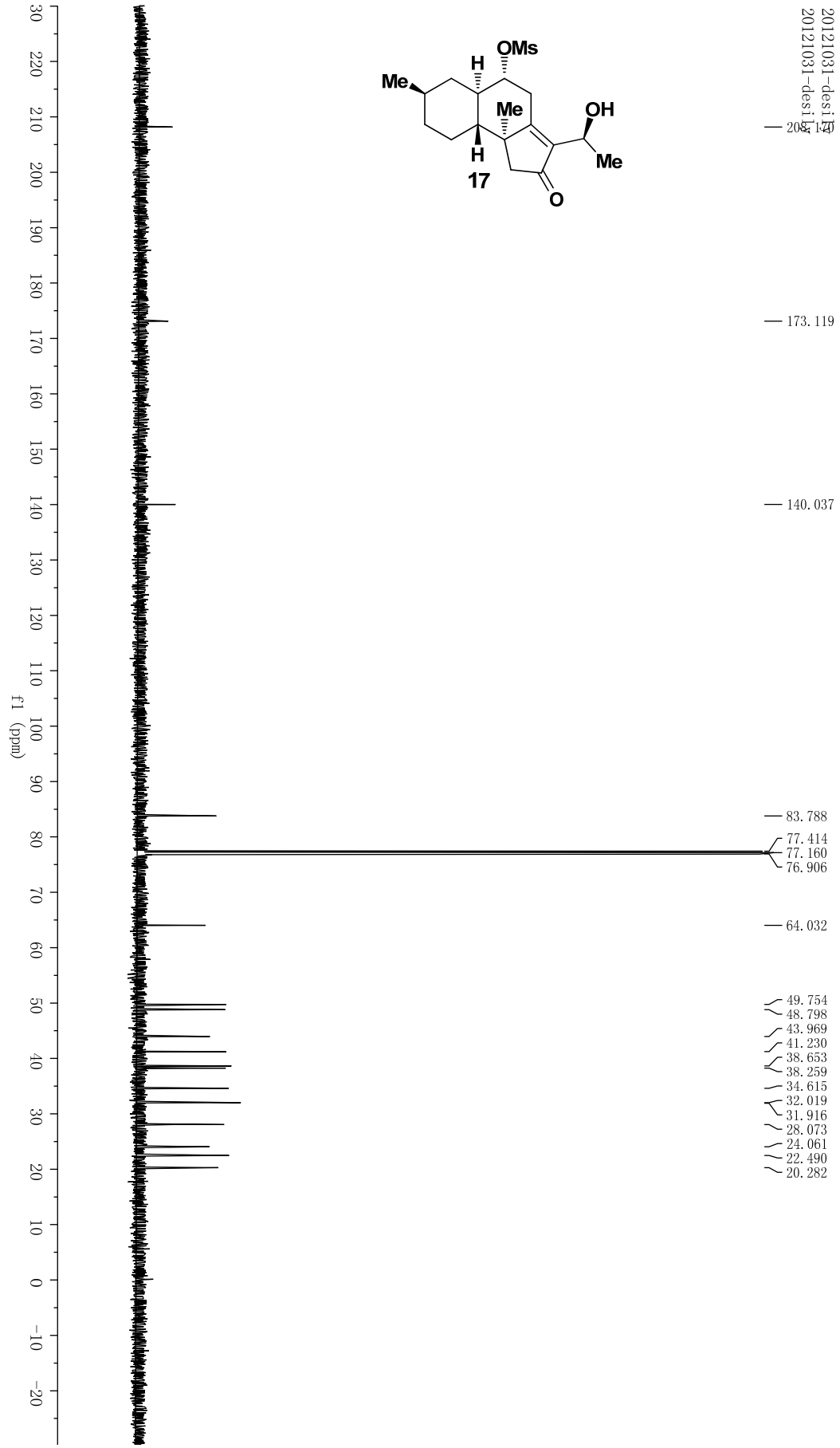
NOESY Spectra of **16**



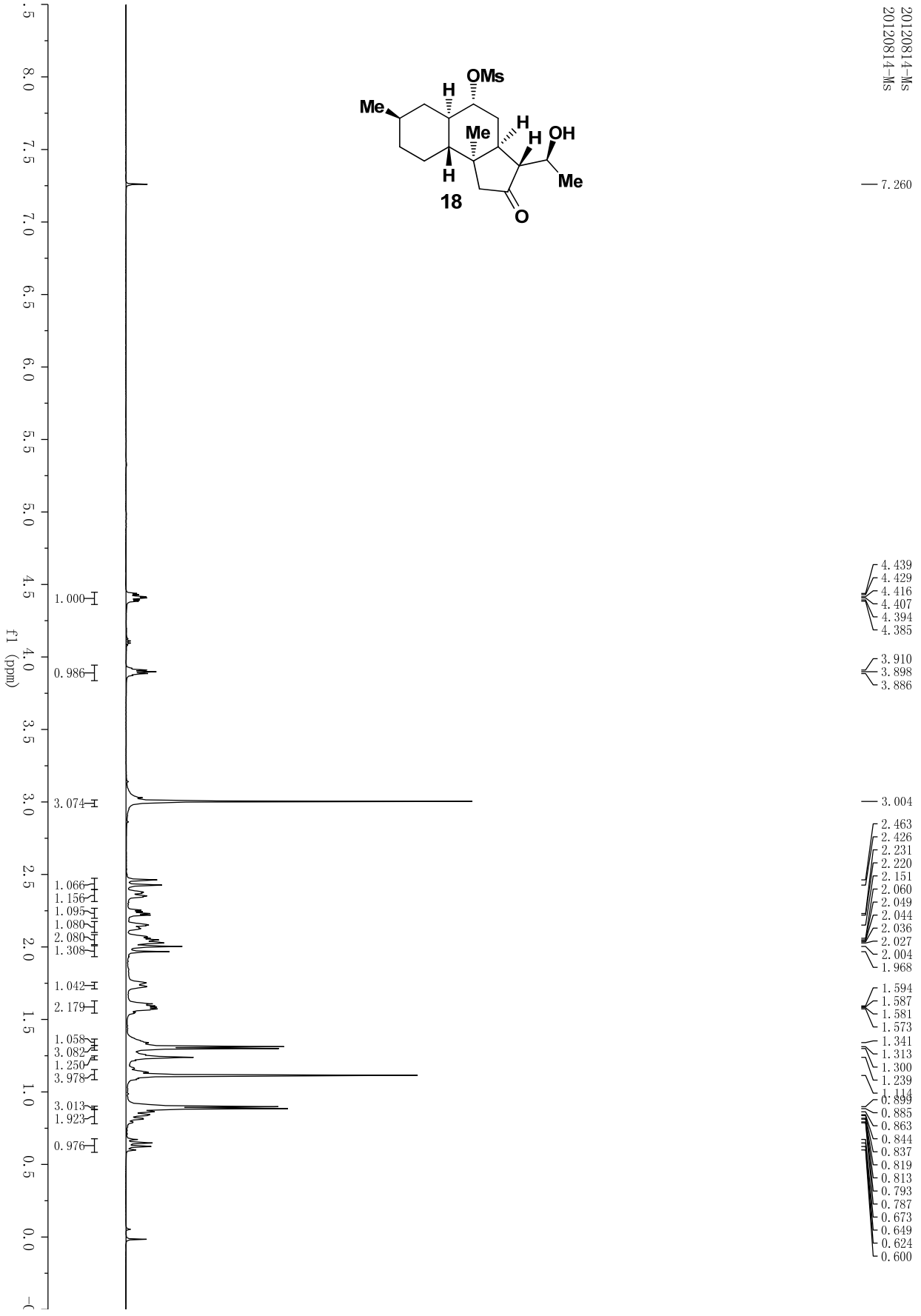
[1] H NMR Spectra of **17**



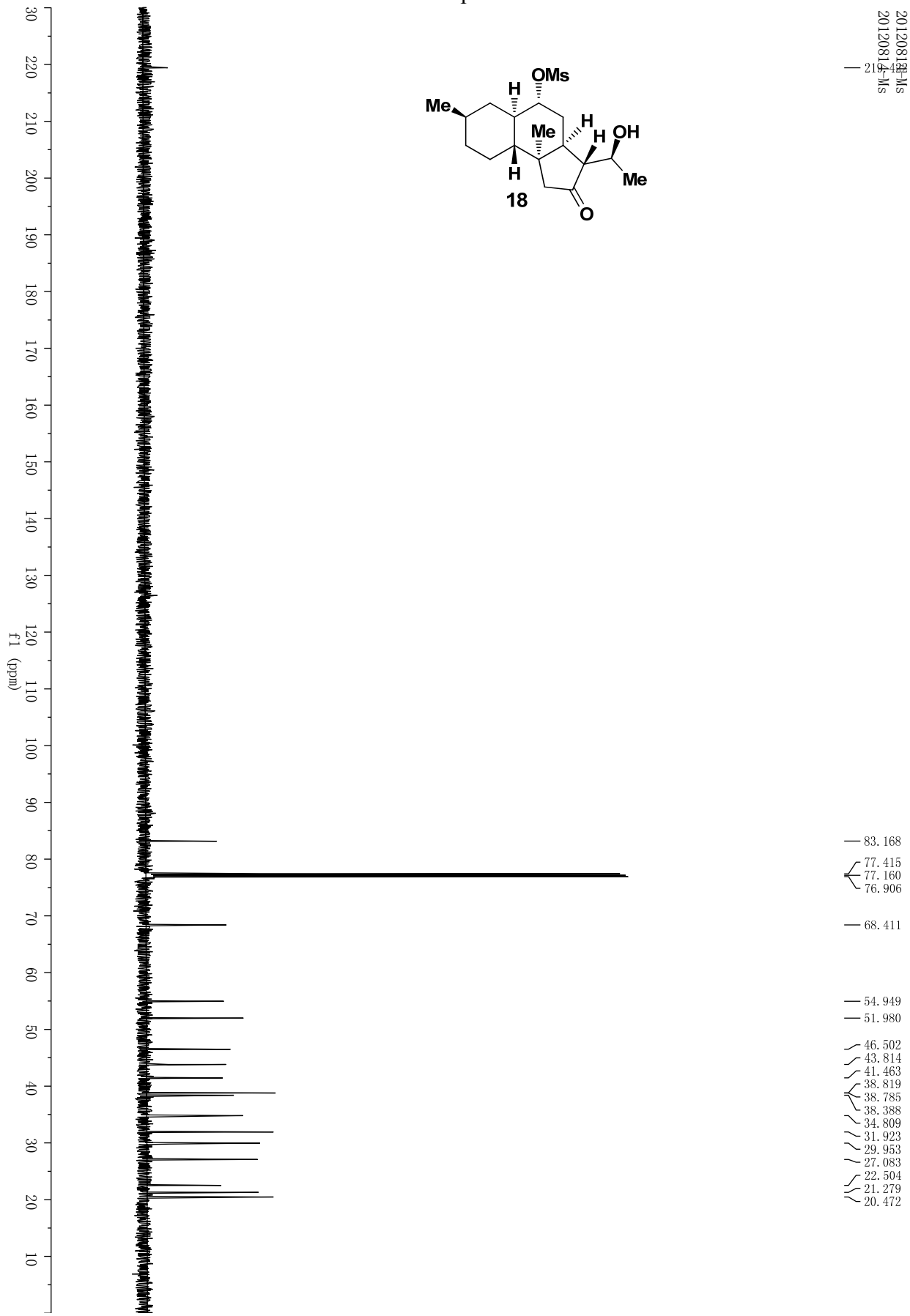
^{13}C NMR Spectra of **17**



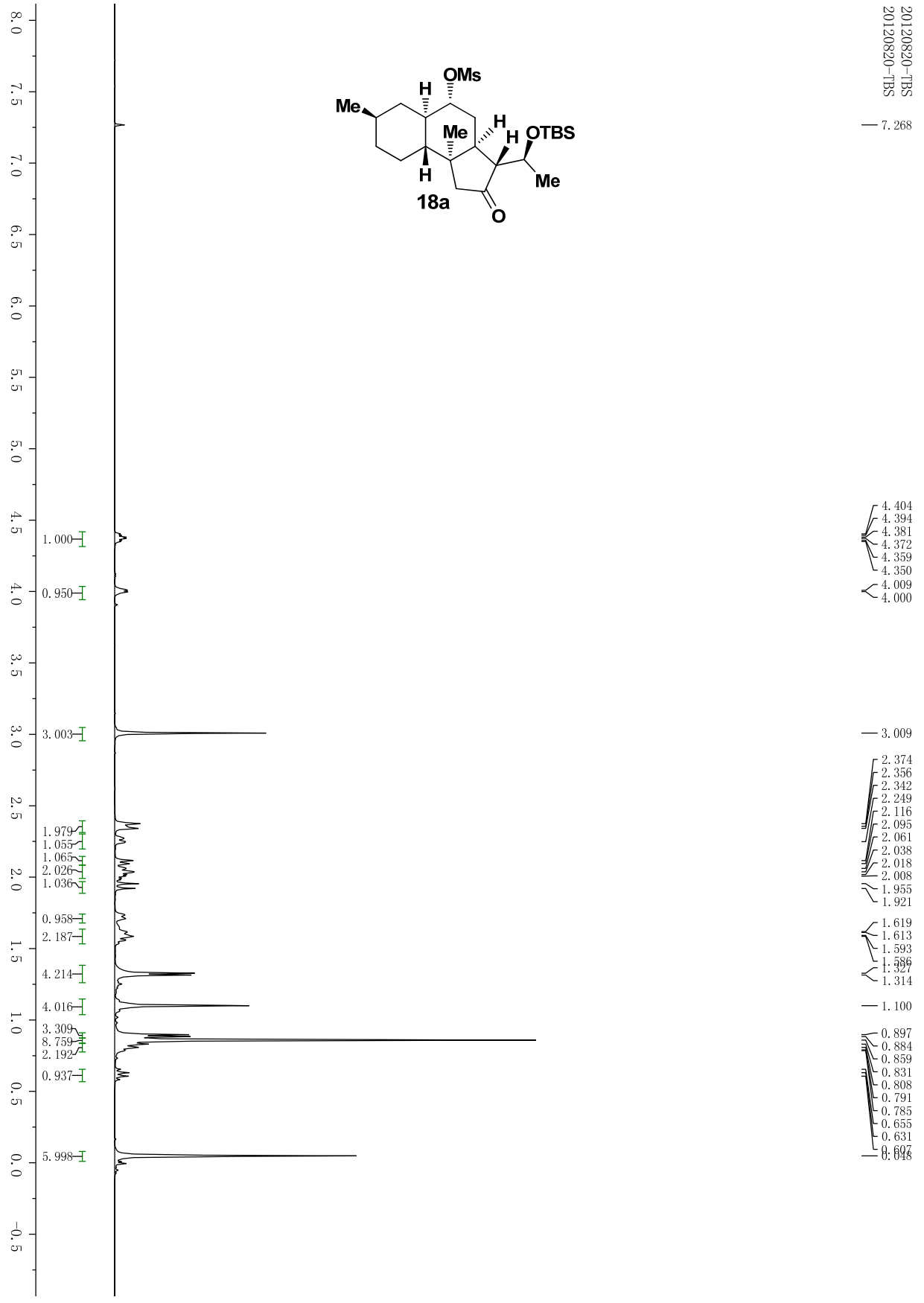
^{1}H NMR Spectra of **18**



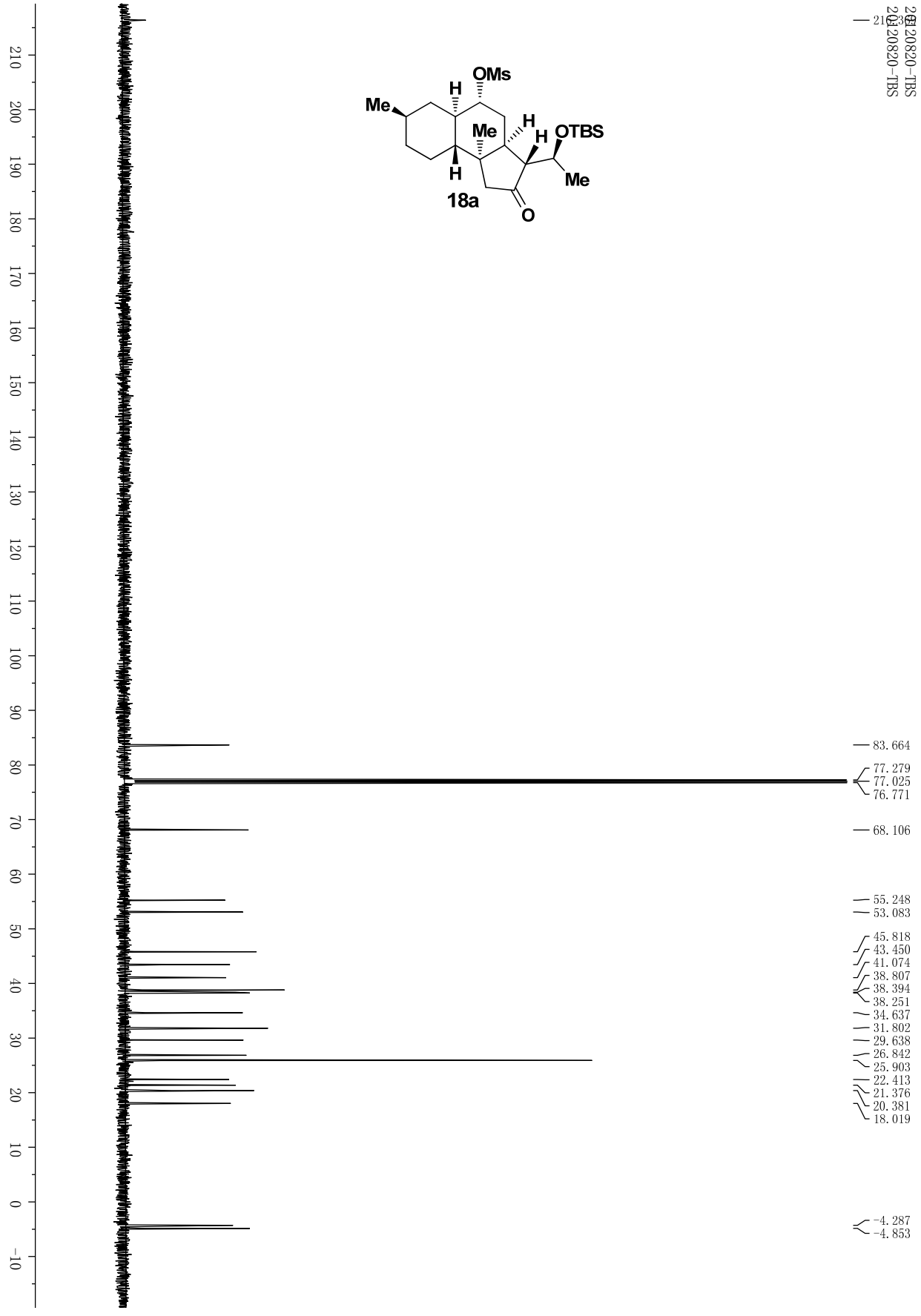
^{13}C NMR Spectra of **18**



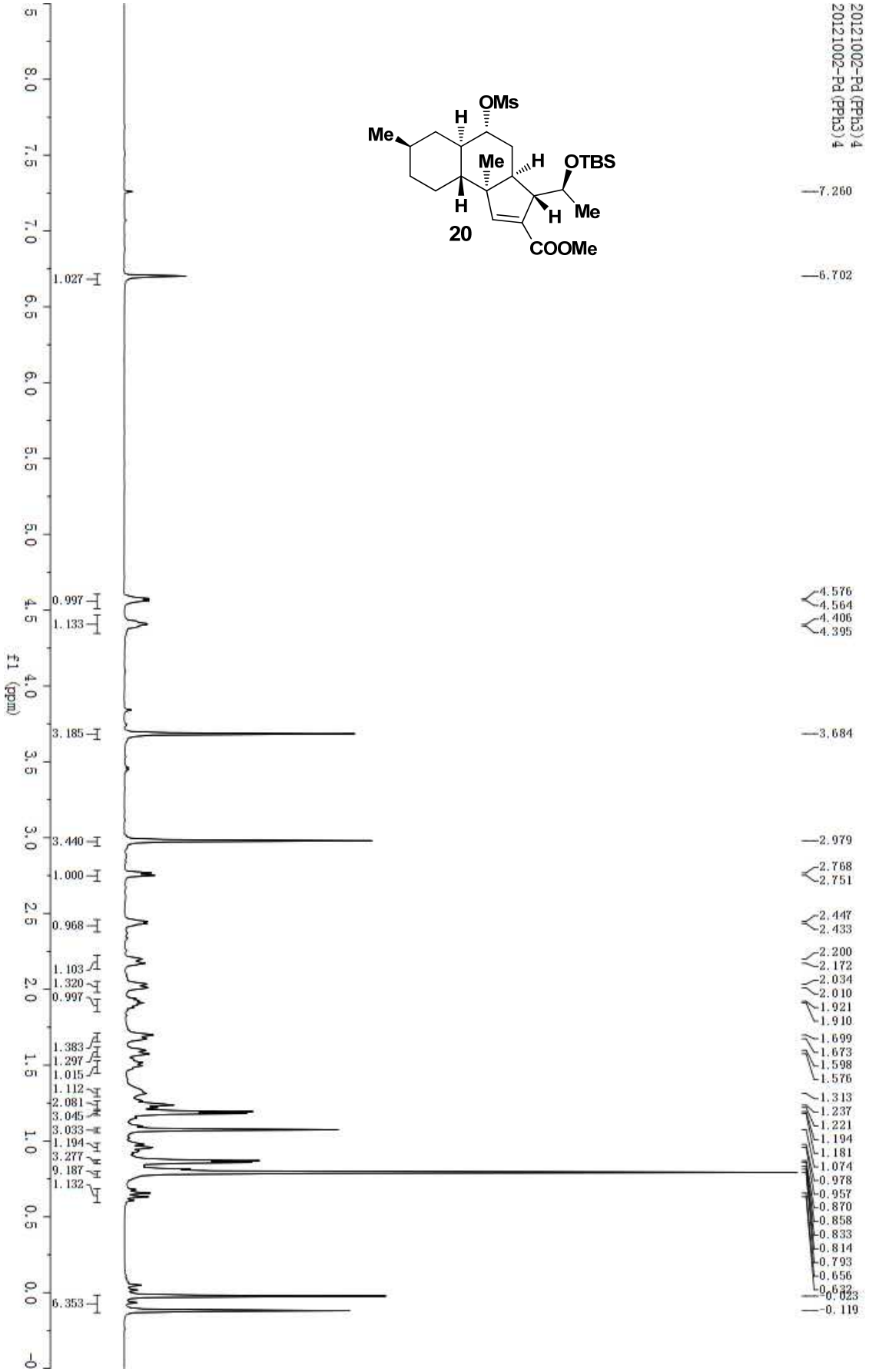
^{1}H NMR Spectra of **18a**



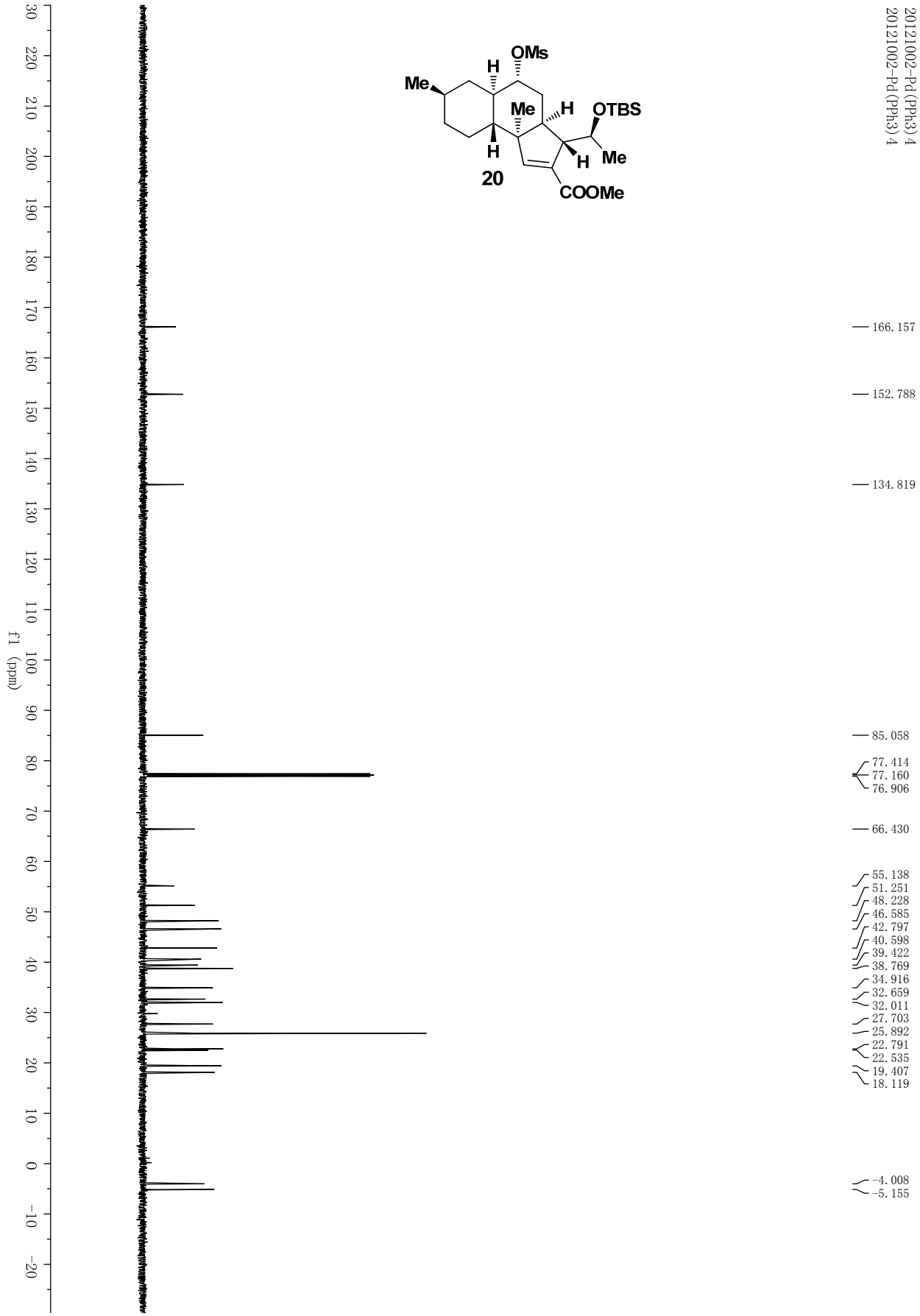
^{13}C NMR Spectra of **18a**



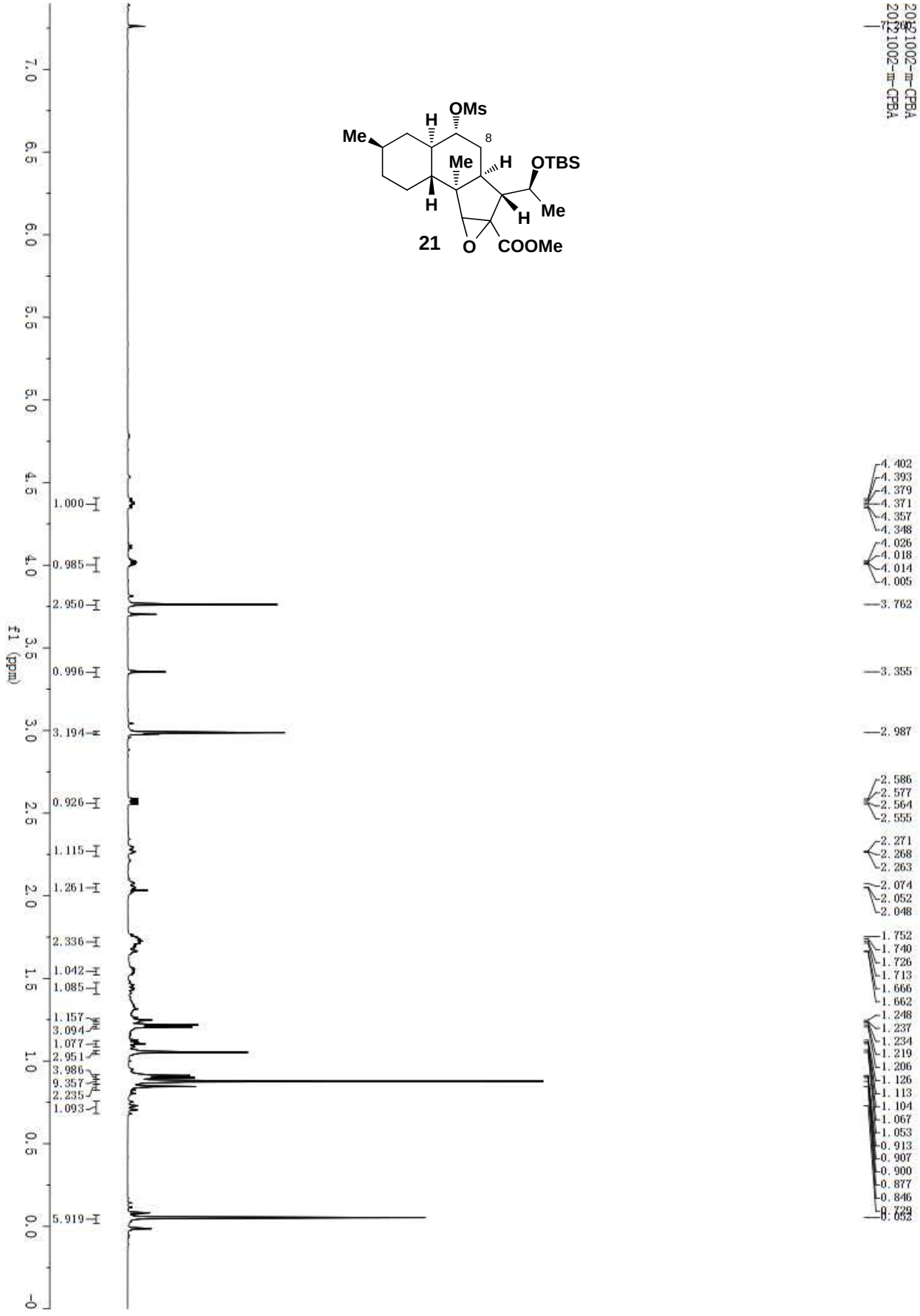
^{1}H NMR Spectra of **20**



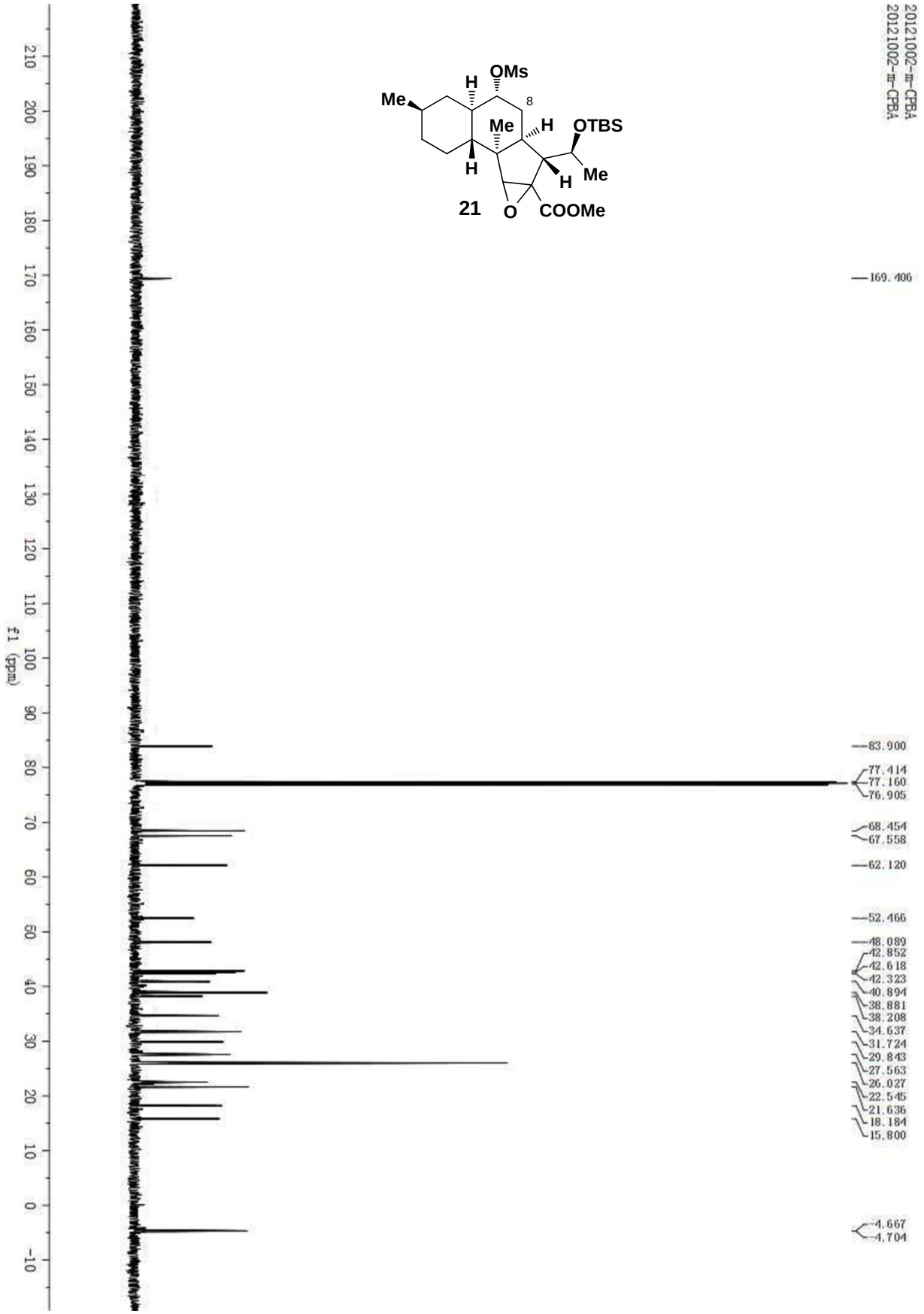
^{13} C NMR Spectra of **20**



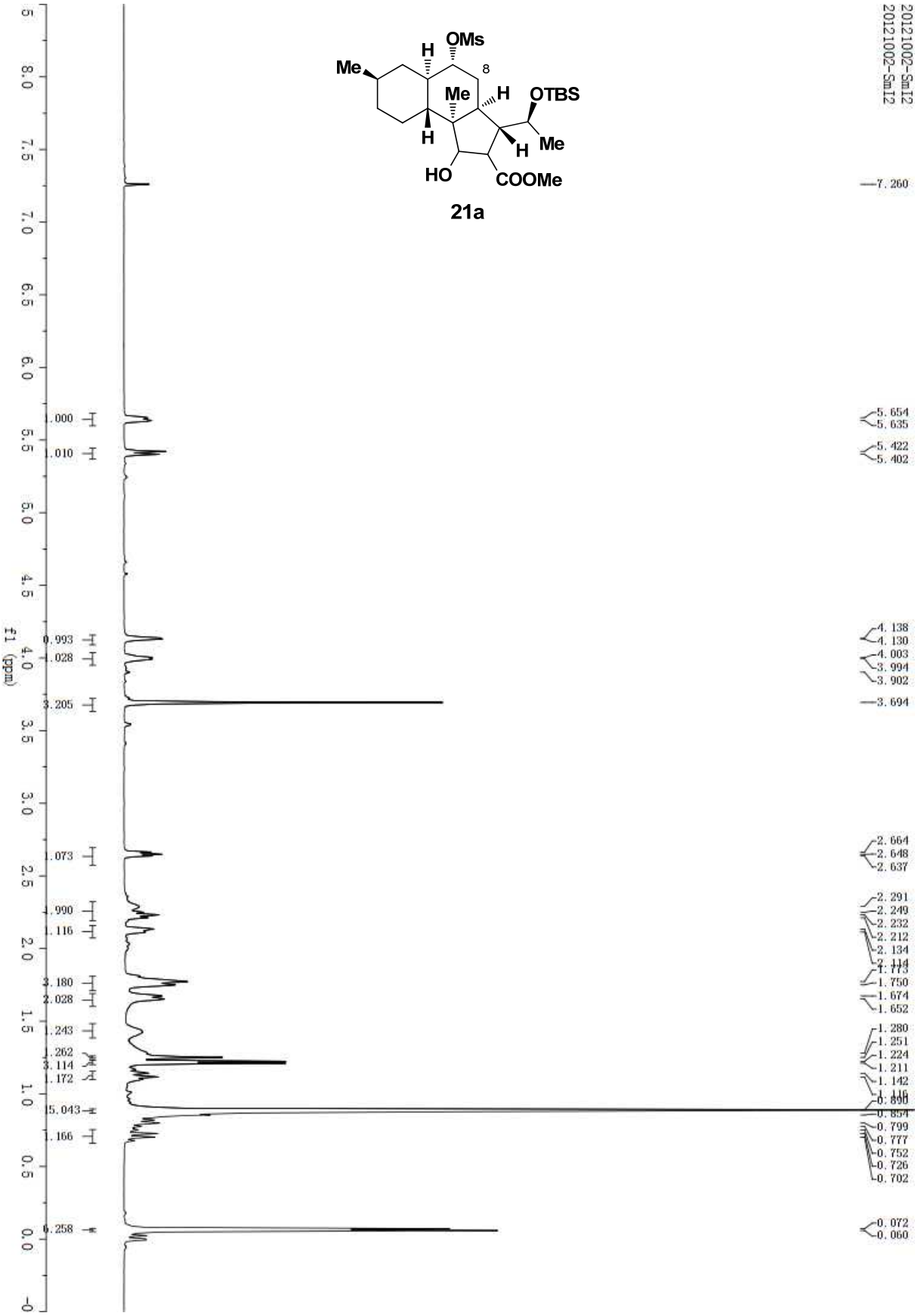
^{1}H NMR Spectra of **21**



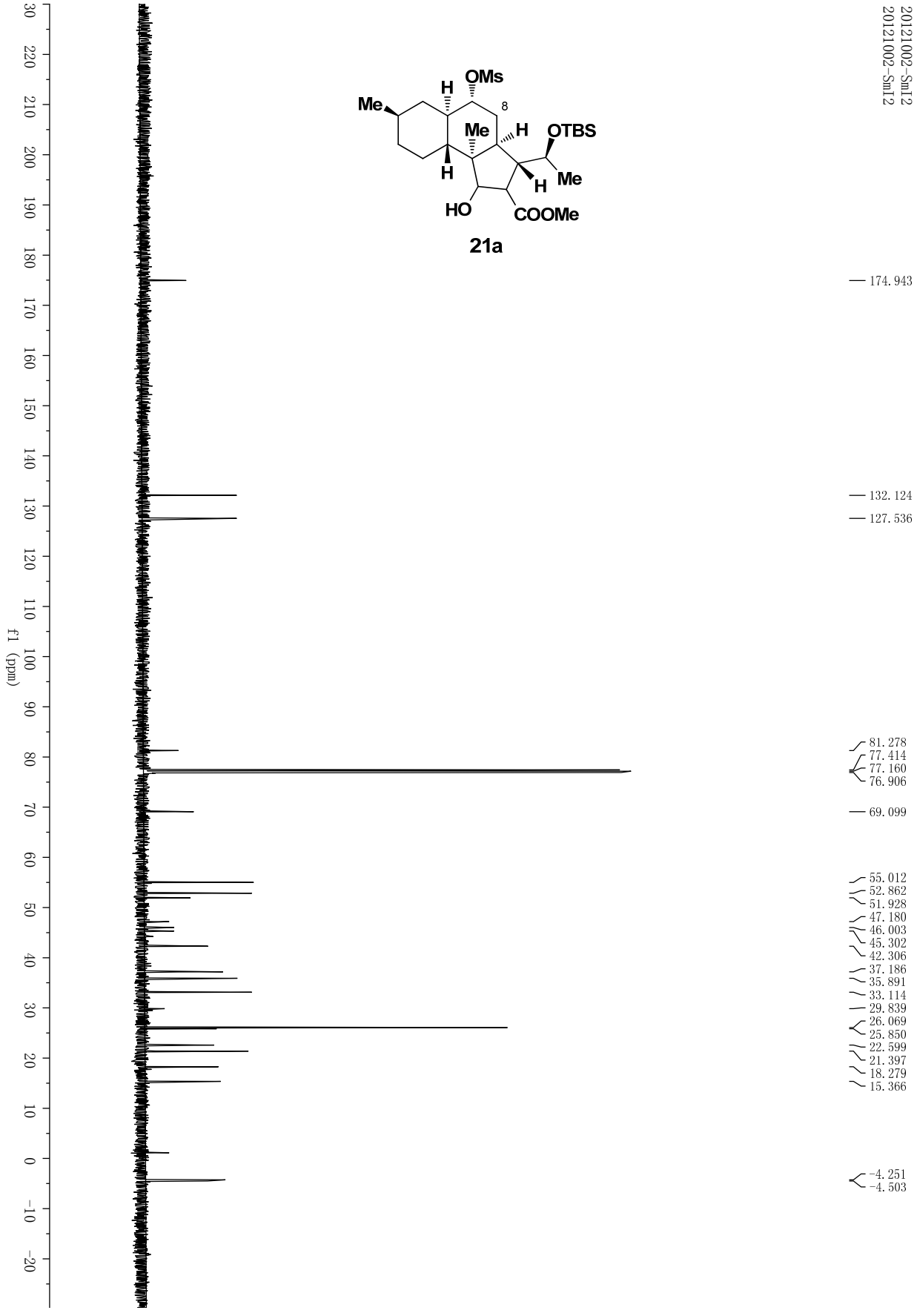
^{13}C NMR Spectra of **21**



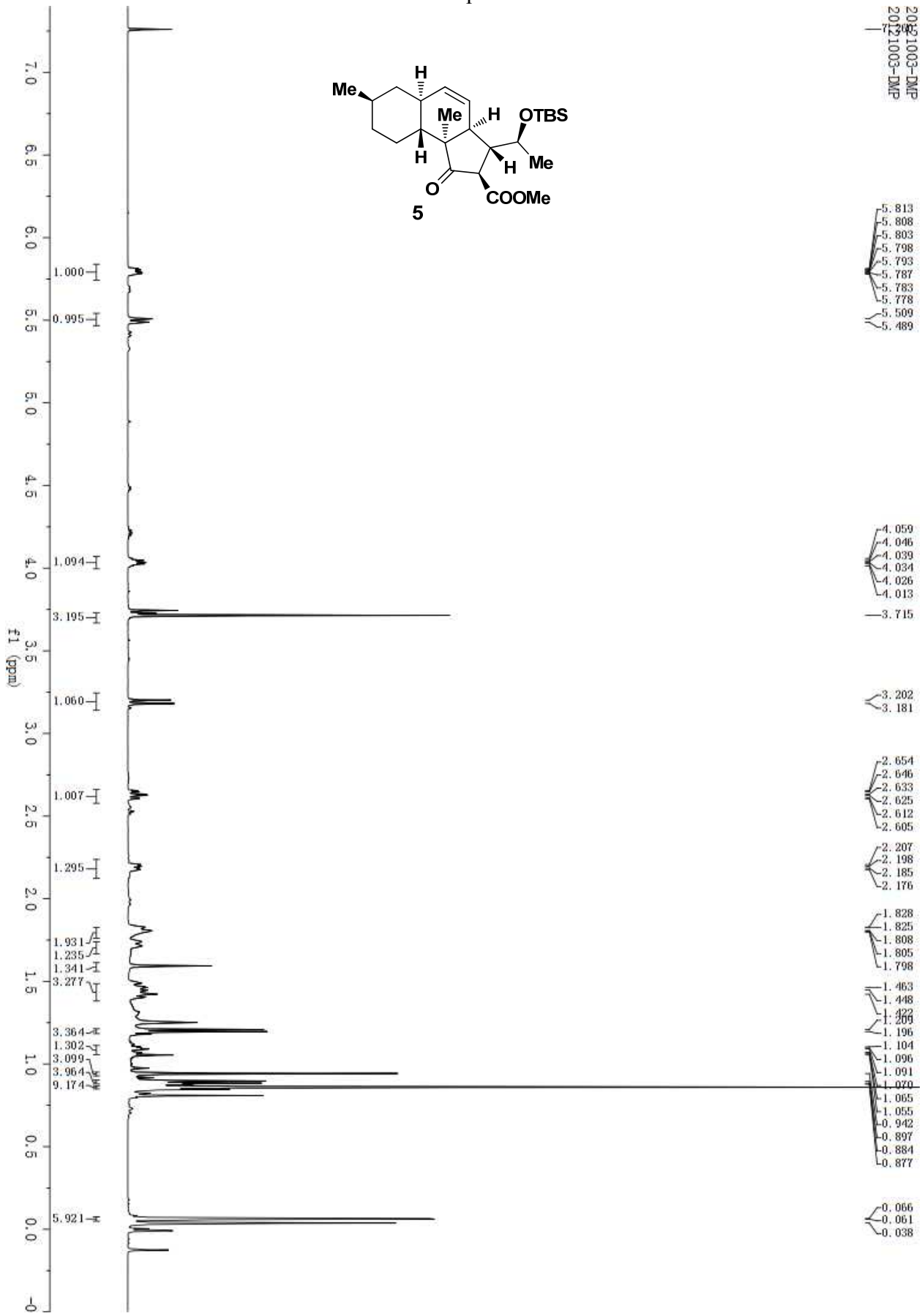
[1] H NMR Spectra of **21a**



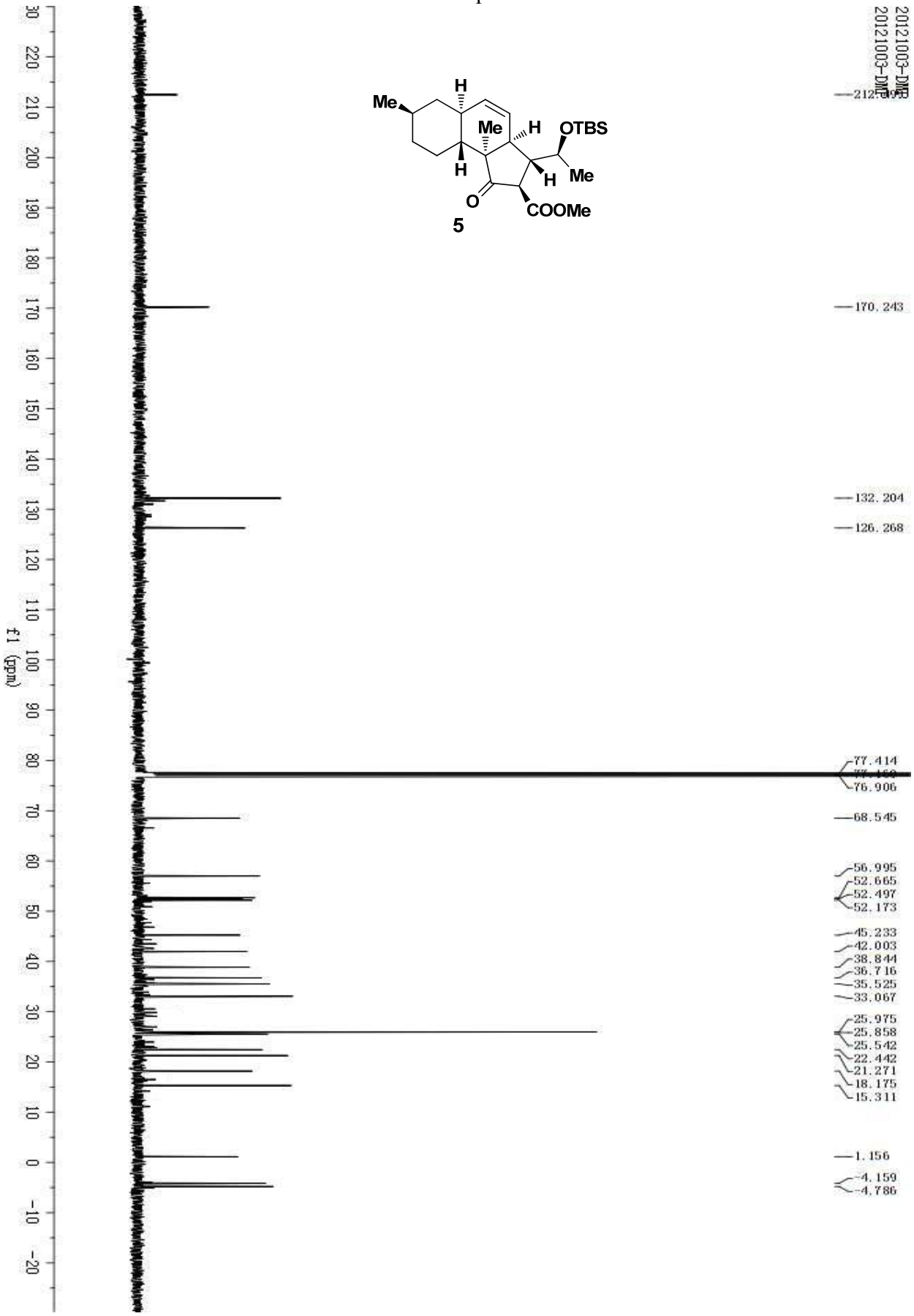
^{13}C NMR Spectra of **21a**



[1] H NMR Spectra of **5**

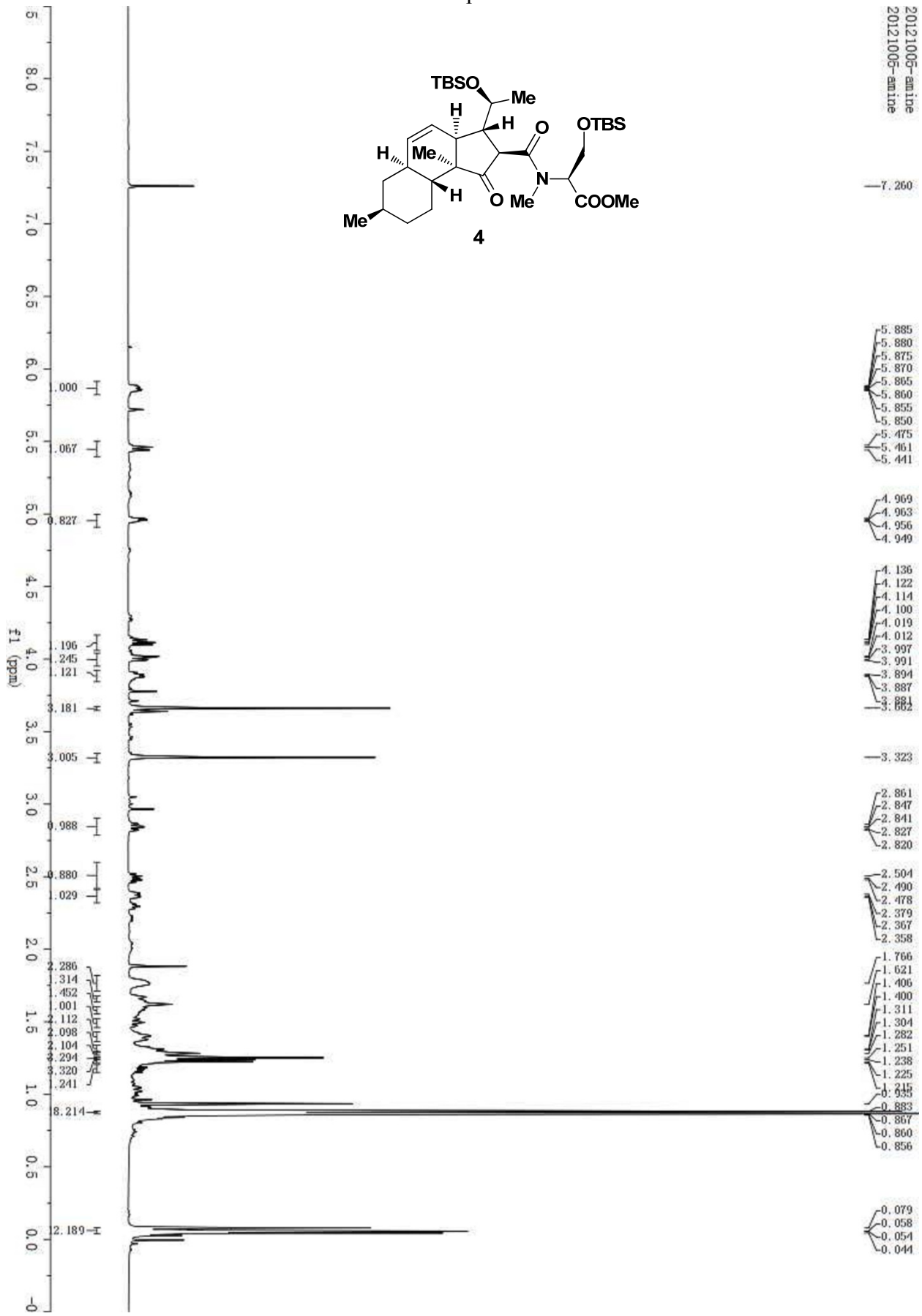


^{13}C NMR Spectra of **5**

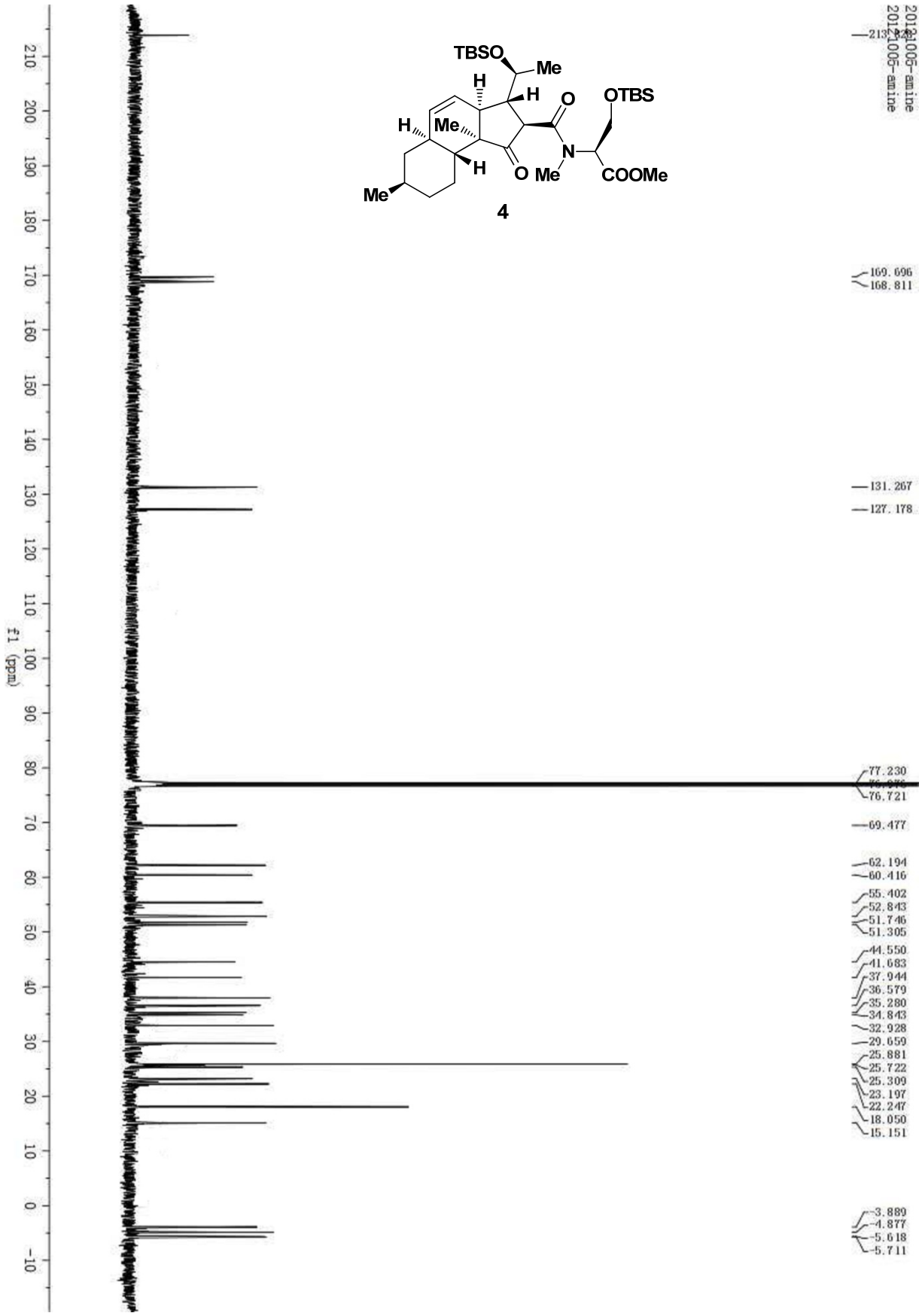


5

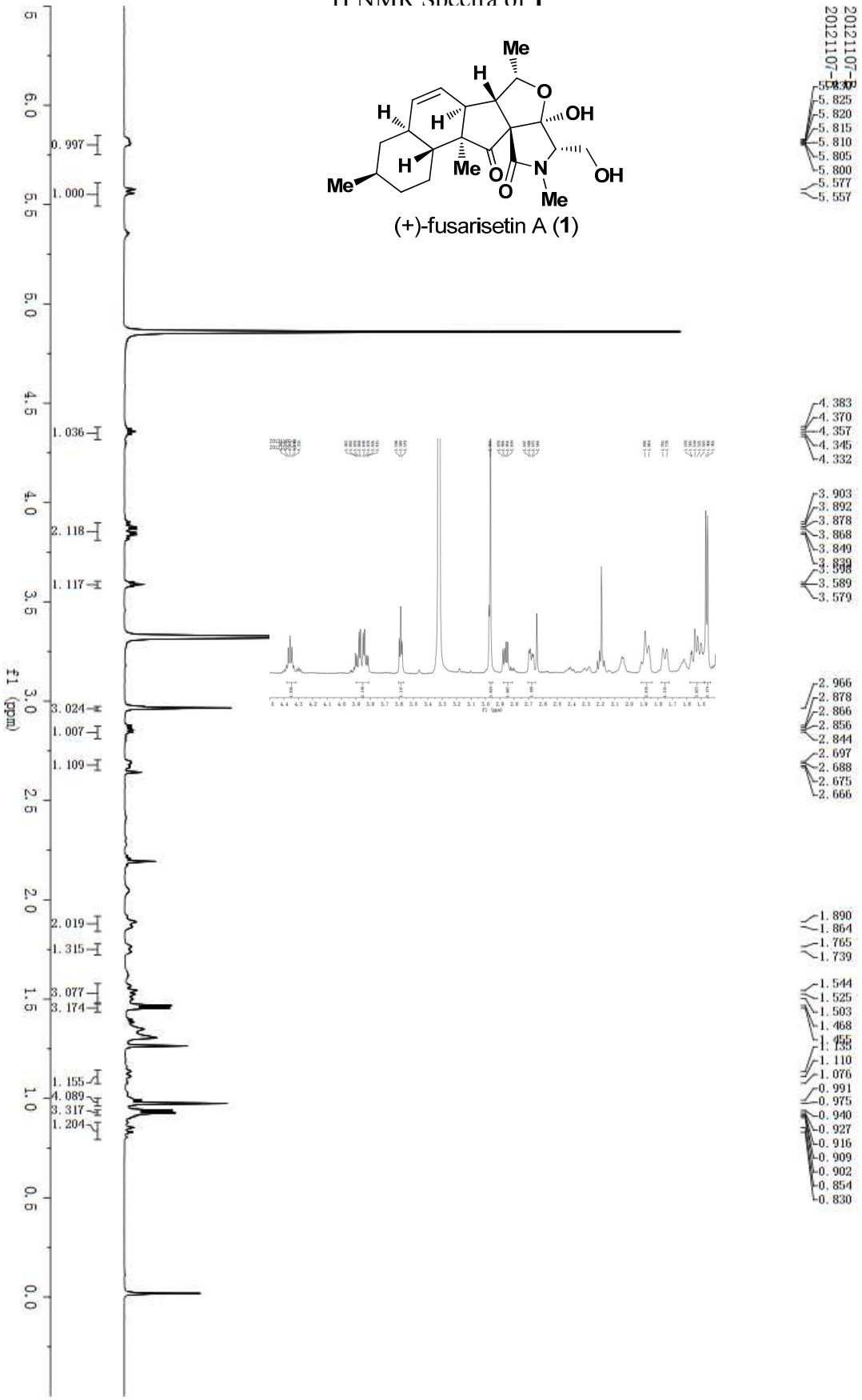
^{1}H NMR Spectra of **4**



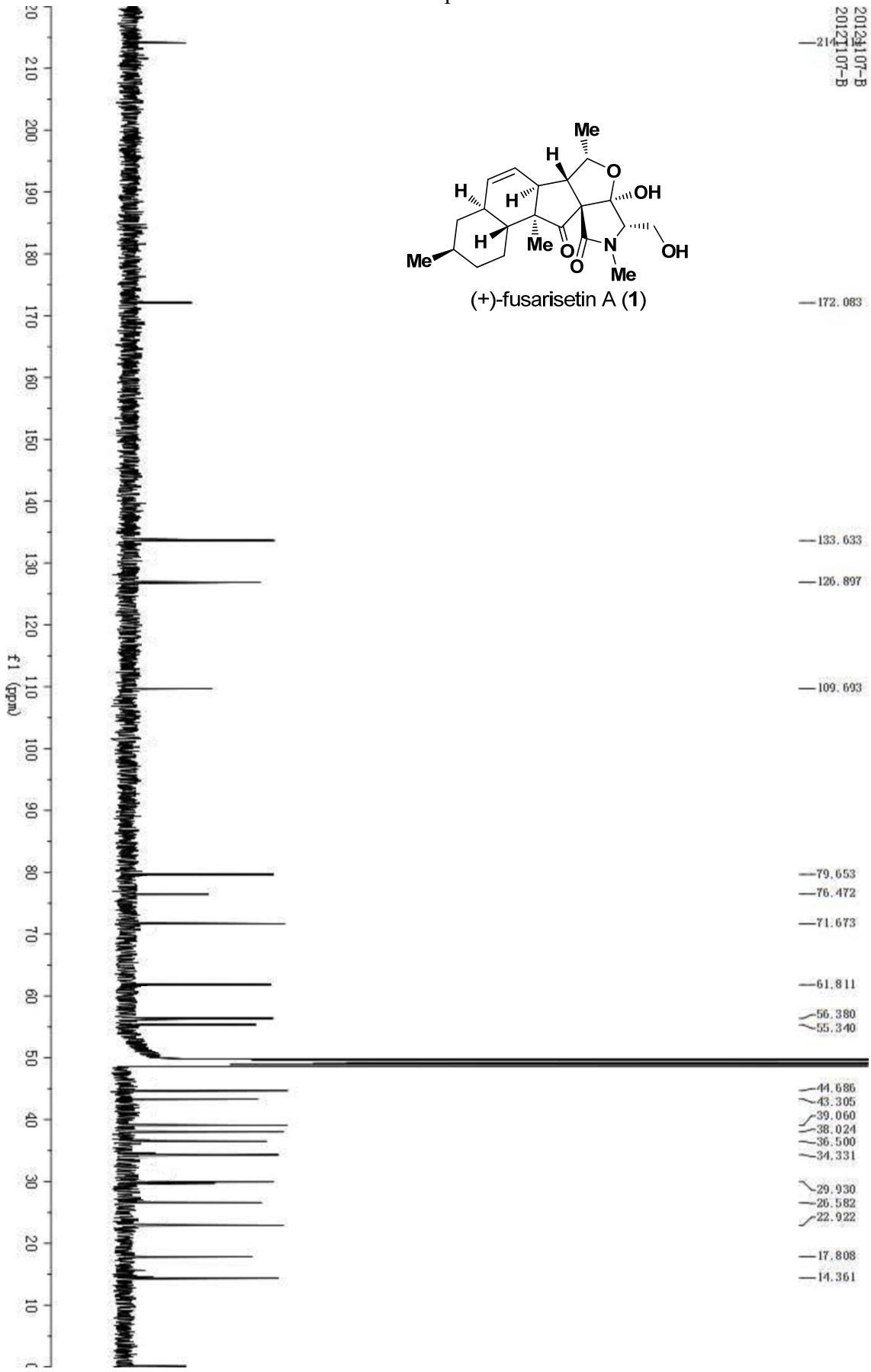
^{13}C NMR Spectra of **4**



^{1}H NMR Spectra of **1**

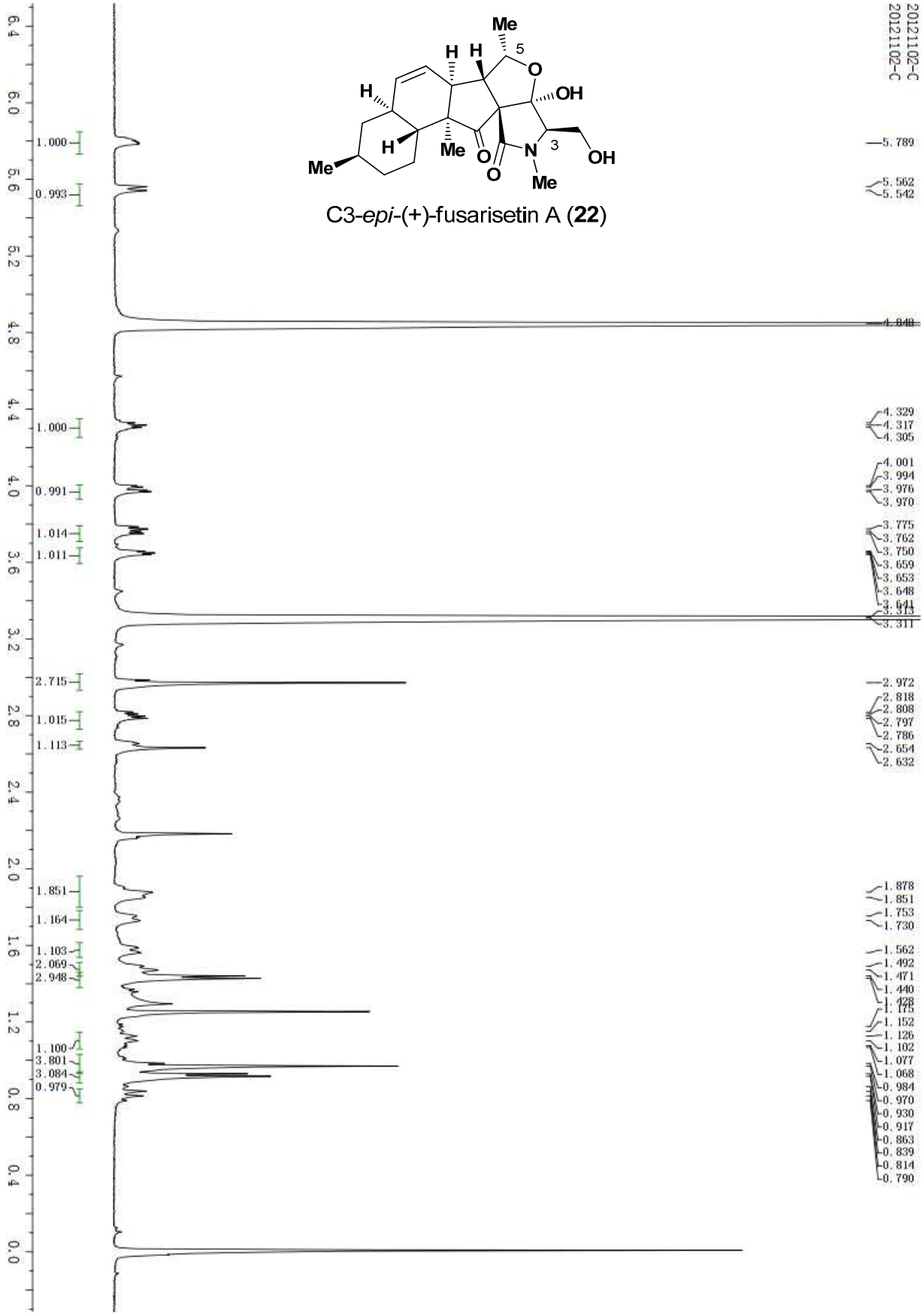


^{13}C NMR Spectra of **1**

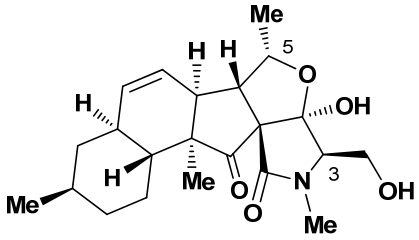


(+)-fusarisetin A (**1**)

[1] H NMR Spectra of **22**



^{13} C NMR Spectra of **22**



C3-*epi*-(+)-fusarisetin A (**22**)